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NEWS	1		Web Page URLs for STN Seminar Schedule - N. America
NEWS	2		"Ask CAS" for self-help around the clock
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NEWS	4	APR 04	STN AnaVist $500 visualization usage credit offered
NEWS	5	MAY 10	CA/CAplus enhanced with 1900-1906 U.S. patent records
NEWS	6	MAY 11	KOREAPAT updates resume
NEWS	7	MAY 19	Derwent World Patents Index to be reloaded and enhanced
NEWS	8	MAY 30	IPC 8 Rolled-up Core codes added to CA/CAplus and USPATFULL/USPAT2
NEWS	9	MAY 30	The F-Term thesaurus is now available in CA/CAplus
NEWS	10	JUN 02	The first reclassification of IPC codes now complete in INPADOC
NEWS	11	JUN 26	TULSA/TULSA2 reloaded and enhanced with new search and and display fields
NEWS	12	JUN 28	Price changes in full-text patent databases EPFULL and PCTFULL
NEWS	13	JUl 11	CHEMSAFE reloaded and enhanced
NEWS	14	JUl 14	FSTA enhanced with Japanese patents
NEWS	15	JUl 19	Coverage of Research Disclosure reinstated in DWPI
NEWS	16	AUG 09	INSPEC enhanced with 1898-1968 archive

NEWS EXPRESS JUNE 30 CURRENT WINDOWS VERSION IS V8.01b, CURRENT MACINTOSH VERSION IS V6.0c(ENG) AND V6.0Jc(JP), AND CURRENT DISCOVER FILE IS DATED 26 JUNE 2006.

NEWS HOURS	STN Operating Hours Plus Help Desk Availability
NEWS LOGIN	Welcome Banner and News Items
NEWS IPC8	For general information regarding STN implementation of IPC 8
NEWS X25	X.25 communication option no longer available

Enter NEWS followed by the item number or name to see news on that specific topic.

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* * * * * * * * * * * * * * * STN Columbus * * * * * * * * * * * * * * * *

FILE 'HOME' ENTERED AT 15:42:04 ON 15 AUG 2006

=> file reg

COST IN U.S. DOLLARS	SINCE FILE ENTRY	TOTAL SESSION
FULL ESTIMATED COST	0.21	0.21

FILE 'REGISTRY' ENTERED AT 15:42:13 ON 15 AUG 2006

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STRUCTURE FILE UPDATES: 14 AUG 2006 HIGHEST RN 901253-54-1
DICTIONARY FILE UPDATES: 14 AUG 2006 HIGHEST RN 901253-54-1

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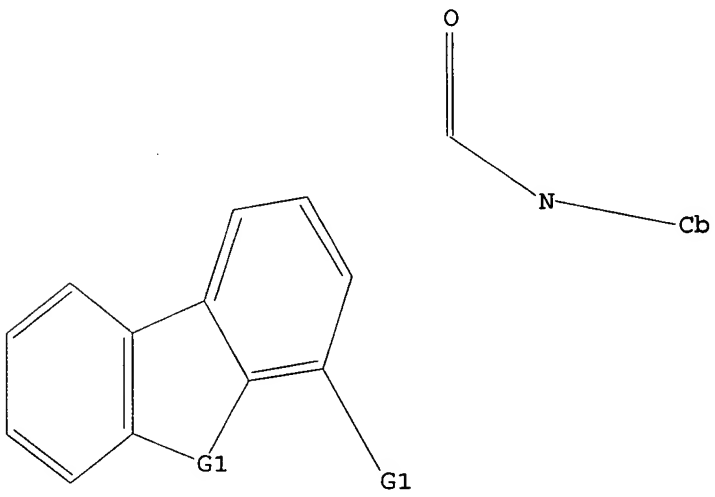
http://www.cas.org/ONLINE/UG/regprops.html

=>
Uploading C:\Documents and Settings\ychu\Desktop\Case\10532273\10532273H.str

L1 STRUCTURE UPLOADED

=> d
L1 HAS NO ANSWERS
L1 STR



G1 O,S

Structure attributes must be viewed using STN Express query preparation.

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SAMPLE SCREEN SEARCH COMPLETED - 2046 TO ITERATE

97.8% PROCESSED 2000 ITERATIONS 0 ANSWERS
INCOMPLETE SEARCH (SYSTEM LIMIT EXCEEDED)
SEARCH TIME: 00.00.01

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FULL FILE PROJECTIONS:  ONLINE  **COMPLETE**
                        BATCH   **COMPLETE**
PROJECTED ITERATIONS:        38207 TO    43633
PROJECTED ANSWERS:               0 TO        0

L2            0 SEA SSS SAM L1

=>
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L3      STRUCTURE UPLOADED

=> d
L3 HAS NO ANSWERS
L3               STR
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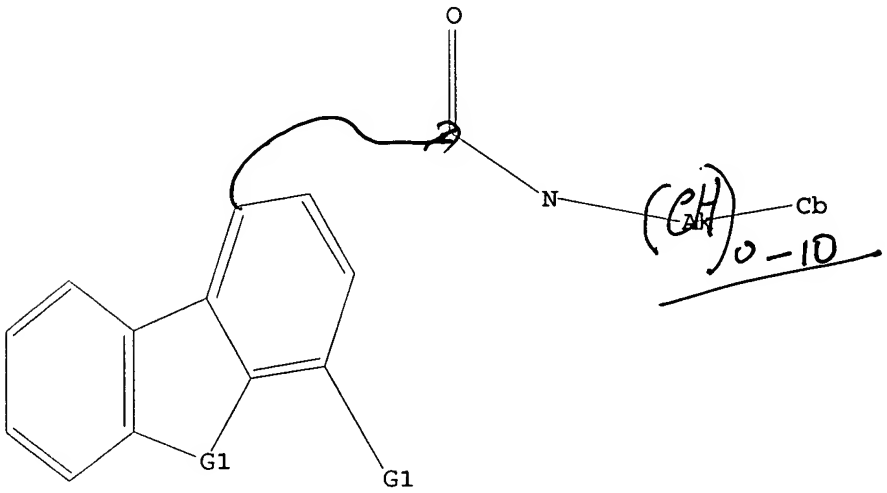


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G1 O,S

Structure attributes must be viewed using STN Express query preparation.

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SAMPLE SCREEN SEARCH COMPLETED -     2045 TO ITERATE

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INCOMPLETE SEARCH (SYSTEM LIMIT EXCEEDED)
SEARCH TIME: 00.00.01

FULL FILE PROJECTIONS:  ONLINE  **COMPLETE**
                        BATCH   **COMPLETE**
PROJECTED ITERATIONS:        38188 TO    43612
PROJECTED ANSWERS:               2 TO      125

L4            2 SEA SSS SAM L3

=> s l4 full
FULL SEARCH INITIATED 15:45:11 FILE 'REGISTRY'
FULL SCREEN SEARCH COMPLETED -    41037 TO ITERATE

100.0% PROCESSED    41037 ITERATIONS                                38 ANSWERS
SEARCH TIME: 00.00.02
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L5            38 SEA SSS FUL L3

=> file caplus
COST IN U.S. DOLLARS                                  SINCE FILE      TOTAL
                                                         ENTRY    SESSION
FULL ESTIMATED COST                                     169.14     169.35

FILE 'CAPLUS' ENTERED AT 15:45:43 ON 15 AUG 2006
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FILE COVERS 1907 - 15 Aug 2006  VOL 145 ISS 8
FILE LAST UPDATED: 14 Aug 2006  (20060814/ED)

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=> s l5
L6            14 L5

=> d ibib abs hitstr tot

L6   ANSWER 1 OF 14  CAPLUS  COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER:         2006:103883  CAPLUS
DOCUMENT NUMBER:          144:170874
TITLE:                    Preparation of dibenzofurans and related compounds as
                          phosphodiesterase type 4 inhibitors useful for the
                          treatment of inflammatory and allergic disorders
INVENTOR(S):              Balasubramanian, Gopalan; Gharat, Laxmikant Atmaram;
                          Joshi, Hemant Vasant
PATENT ASSIGNEE(S):       Glenmark Pharmaceuticals Ltd., India
SOURCE:                   PCT Int. Appl., 145 pp.
                          CODEN: PIXXD2
DOCUMENT TYPE:            Patent
LANGUAGE:                 English
FAMILY ACC. NUM. COUNT:   1
PATENT INFORMATION:

     PATENT NO.           KIND   DATE        APPLICATION NO.          DATE
     --------------       ----   --------    --------------------     --------
     WO 2006011024         A2    20060202    WO 2005-IB2061           20050718
     WO 2006011024         A3    20060330
         W:  AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH,
             CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD,
             GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KP, KR, KZ,
             LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA,
             NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK,
             SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU,
             ZA, ZM, ZW
         RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE,
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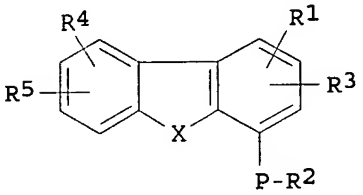
Not ODP Not 102(E)

IS, IT, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM

PRIORITY APPLN. INFO.: US 2004-589479P P 20040719
IN 2004-MU809 A 20040729

OTHER SOURCE(S): MARPAT 144:170874

GI



I

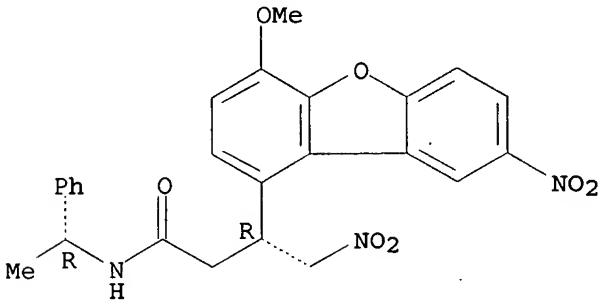
AB The present invention relates to novel tricyclic compds. (shown as I; variables defined below; e.g. 4-(4-methoxydibenzofuran-1-yl)-2-pyrrolidinone), analogs, tautomers, regioisomers, stereoisomers, enantiomers, diastereomers, polymorphs, pharmaceutically acceptable salts, appropriate oxides, pharmaceutically acceptable solvates and pharmaceutical compns. contg. them. The present invention also relates to phosphodiesterase type 4 (PDE4) inhibitors which down regulate or inhibit the prodn. of TNF-.alpha. and therefore are useful in the treatment of variety of allergic and inflammatory diseases including asthma and chronic obstructive pulmonary disease (COPD). Methods of prepn. are claimed and prepns. and/or characterization data for .apprx.60 examples of I are included. For example, 4-(4-methoxydibenzofuran-1-yl)-2-pyrrolidinone was prepd. by reductive cyclization of 3-(4-methoxydibenzofuran-1-yl)-4-nitrobutanoate (prepn. given) in iPrOH/DMF using 10 % Pd/C. For I: R1 is (un)substituted aryl, arylalkyl, heteroaryl, heterocyclyl, heterocyclylalkyl, or heteroarylalkyl; R2, R3, R4, R5 and R6 may be the same or different and = H or (un)substituted alkyl, alkenyl, alkynyl, cycloalkyl, cycloalkylalkyl, cycloalkenyl, aryl, arylalkyl, heteroaryl, heterocyclic group, heterocyclylalkyl, or heteroarylalkyl, -NR8R9, -C(O)R8, -C(O)OR8, -C(O)NR8R9, -S(O)mR8, -S(O)mNR8R9, nitro, -OH, cyano, formyl, acetyl, halogen, -OR8, -SR8, or a protecting group, or when R1 and R3, or R4 and R5 are ortho to each other then R1 and R3 together with the C atoms to which they are bound or R4 and R5 together with the C atoms to which they are bound may be joined to a form a (un)satd. cyclic ring, which may optionally include up to two heteroatoms = O, NRa or S; X is O, S(O)m and NR6; P is O or S; m = 0-2; addnl. details are given in the claims. IC50 values for inhibition of PDE4 by .apprx.60 examples of I are tabulated.

IT 874673-67-3P, N-((1R)-1-Phenylethyl)-(3R)-3-(4-methoxy-8-nitrodibenzofuran-1-yl)-4-nitrobutanamide 874673-68-4P, N-((1R)-1-Phenylethyl)-(3R)-3-(8-amino-4-methoxydibenzofuran-1-yl)-4-nitrobutanamide 874673-69-5P, N-((1R)-1-Phenylethyl)-(3R)-3-[4-methoxy-8-[(methylsulfonyl)amino]dibenzofuran-1-yl]-4-nitrobutanamide 874673-70-8P, N-((1R)-1-Phenylethyl)-(3S)-3-[4-methoxy-8-[(methylsulfonyl)amino]dibenzofuran-1-yl]-4-nitrobutanamide 874673-74-2P, N-((1R)-1-Phenylethyl)-(3R)-3-(4-methoxydibenzofuran-1-yl)-4-nitrobutanamide 874673-75-3P, N-((1R)-1-Phenylethyl)-(3S)-3-(4-methoxydibenzofuran-1-yl)-4-nitrobutanamide 874673-79-7P, N-((1R)-1-Phenylethyl)-(3R)-3-[4-(difluoromethoxy)dibenzofuran-1-yl]-4-nitrobutanamide 874673-80-0P, N-((1R)-1-Phenylethyl)-(3S)-3-[4-(difluoromethoxy)dibenzofuran-1-yl]-4-nitrobutanamide
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT

(Reactant or reagent)
(prepn. of dibenzofurans and related compds. as phosphodiesterase type 4 inhibitors useful for treatment of inflammatory and allergic disorders)

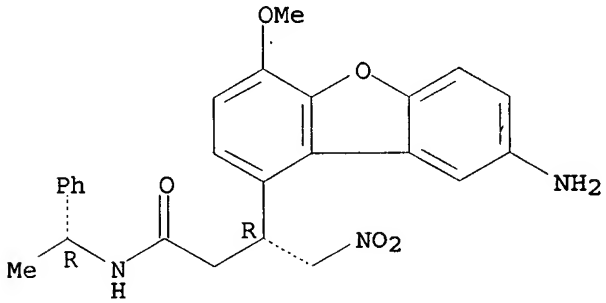
RN 874673-67-3 CAPLUS
CN 1-Dibenzofuranpropanamide, 4-methoxy-8-nitro-.beta.-(nitromethyl)-N-[(1R)-1-phenylethyl]-, (.beta.R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



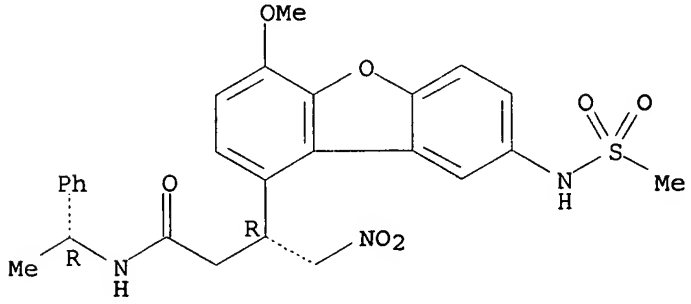
RN 874673-68-4 CAPLUS
CN 1-Dibenzofuranpropanamide, 8-amino-4-methoxy-.beta.-(nitromethyl)-N-[(1R)-1-phenylethyl]-, (.beta.R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



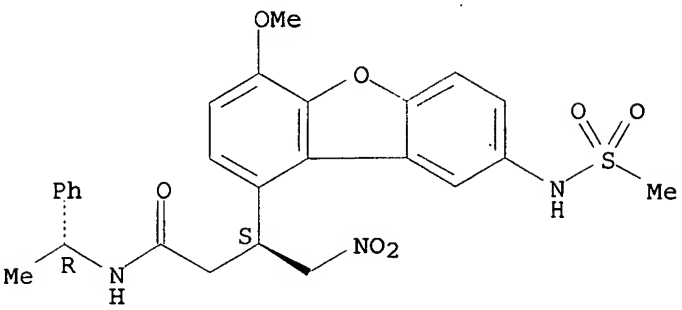
RN 874673-69-5 CAPLUS
CN 1-Dibenzofuranpropanamide, 4-methoxy-8-[(methylsulfonyl)amino]-.beta.-(nitromethyl)-N-[(1R)-1-phenylethyl]-, (.beta.R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



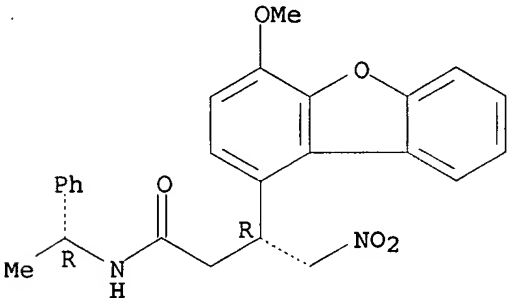
RN 874673-70-8 CAPLUS
CN 1-Dibenzofuranpropanamide, 4-methoxy-8-[(methylsulfonyl)amino]-.beta.-(nitromethyl)-N-[(1R)-1-phenylethyl]-, (.beta.S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



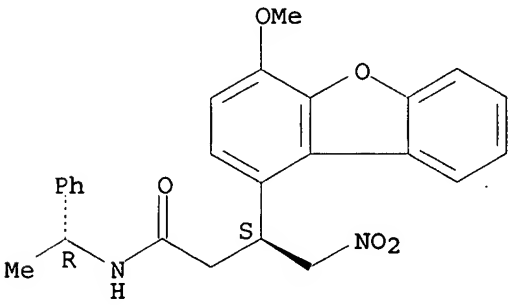
RN 874673-74-2 CAPLUS
CN 1-Dibenzofuranpropanamide, 4-methoxy-.beta.-(nitromethyl)-N-[(1R)-1-phenylethyl]-, (.beta.R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



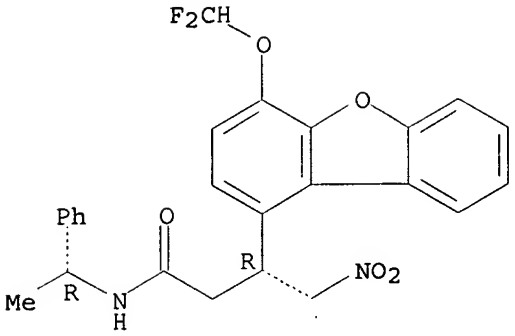
RN 874673-75-3 CAPLUS
CN 1-Dibenzofuranpropanamide, 4-methoxy-.beta.-(nitromethyl)-N-[(1R)-1-phenylethyl]-, (.beta.S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



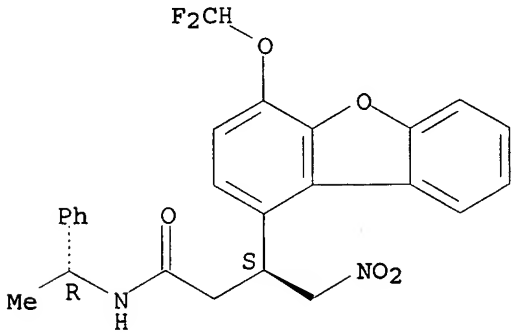
RN 874673-79-7 CAPLUS
CN 1-Dibenzofuranpropanamide, 4-(difluoromethoxy)-.beta.-(nitromethyl)-N-[(1R)-1-phenylethyl]-, (.beta.R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 874673-80-0 CAPLUS
CN 1-Dibenzofuranpropanamide, 4-(difluoromethoxy)-.beta.-(nitromethyl)-N-[(1R)-1-phenylethyl]-, (.beta.S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L6 ANSWER 2 OF 14 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2005:99226 CAPLUS
DOCUMENT NUMBER: 142:197859
TITLE: Preparation of dibenzo[b,f]furan-1-carboxamides, 9H-carbazole-4-carboxamides, and dibenzo[b,d]thiophene-4-carboxamides as PDE4 inhibitors for the treatment of inflammatory and allergic disorders
INVENTOR(S): Gopalan, Balasubramanian; Gharat, Laxmikant A.; Lakdawala, Aftab D.; Karunakaran, Usha
PATENT ASSIGNEE(S): Glenmark Pharmaceuticals, Inc. USA, USA
SOURCE: U.S. Pat. Appl. Publ., 59 pp., Cont.-in-part of Appl. No. PCT/IB04/000355.
CODEN: USXXCO
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

ODP

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 2005027129	A1	20050203	US 2004-821642	20040409
WO 2004089940	A1	20041021	WO 2004-IB355	20040211

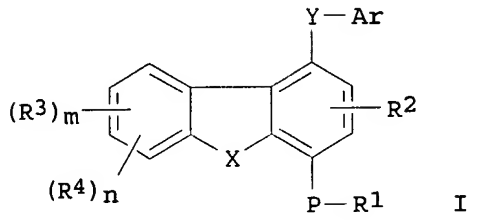
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW
RW: BW, GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ,

BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

PRIORITY APPLN. INFO.: IN 2003-MU363 A 20030411
US 2003-519967P P 20031113
WO 2004-IB355 A2 20040211

OTHER SOURCE(S): MARPAT 142:197859

GI



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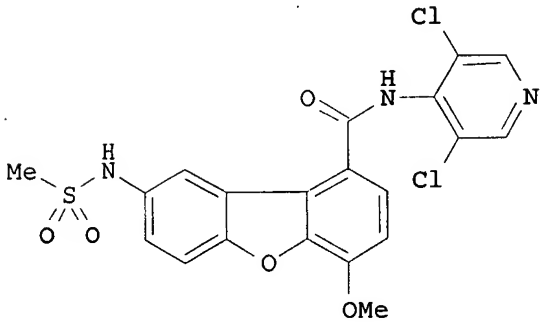


II

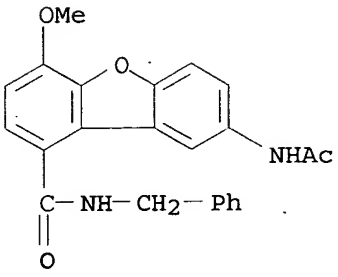
AB Title heterocyclic tricycles I [wherein R1-R3, R5, R6, Ra = independently H, (un)substituted (cyclo)alkyl, (cyclo)alkenyl, alkynyl, (hetero)aryl, heterocyclyl(alkyl), etc.; R4 = NR5R6 (R5, R6 = H, alkyl, cycloalkyl, etc.), heterocyclyl; Ar = (un)substituted aryl(alkyl), heterocyclyl, heteroaryl; X = O, SO0-2, NRa; Y = CONR7, NR7SO0-2, SO0-2NR7, NR7CO; R7 = H, OH, ORa, (un)substituted alkyl, aryl, heterocyclyl; P = O, S; m = 0-3; n = 1-4; Ra = H, alkyl, cycloalkyl, etc.; and tautomers, regioisomers, stereoisomers, enantiomers, diastereomers, polymorphs, N-oxides, pharmaceutically acceptable salts, solvates, and compns. thereof] were prepd. as phosphodiesterase type 4 (PDE4) inhibitors. For example, N-(3,5-dichloropyrid-4-yl)-4-methoxy-8-aminodibenzo[b,f]furan-1-carboxamide (prepd. in six steps from isovanillin, 4-fluoronitrobenzene, and 4-amino-3,5-dichloropyridine) was coupled with methanesulfonyl chloride in THF and pyridine to give the sulfonamide II. The latter inhibited the PDE4-induced conversion of [3H] cAMP to the corresponding [3H] 5'-AMP with IC50 of 0.5058 nM. Thus, I and their pharmaceutical compns. are useful for the treatment of immune disorders, inflammatory conditions, allergic conditions, CNS diseases, and insulin resistant diabetes (no data).

IT 778576-80-0P, N-Benzyl-4-methoxy-8-acetamidodibenzo[b,d]furan-1-carboxamide
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(PDE4 inhibitor; prepn. of tricyclic heterocycles as PDE4 inhibitors for treatment of immune and inflammatory disorders and insulin resistant diabetes)

RN 778576-80-0 CAPLUS

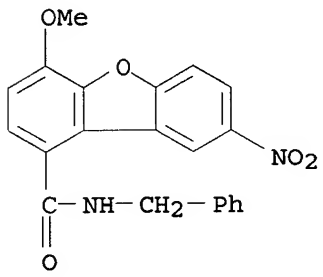
CN 1-Dibenzofurancarboxamide, 8-(acetylamino)-4-methoxy-N-(phenylmethyl)-

(9CI) (CA INDEX NAME)



IT 778576-81-1P, N-Benzyl-4-methoxy-8-nitrodibenzo[b,d]furan-1-carboxamide 778576-82-2P, N-Benzyl-4-methoxy-8-aminodibenzo[b,d]furan-1-carboxamide
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(intermediate; prepn. of tricyclic heterocycles as PDE4 inhibitors for treatment of immune and inflammatory disorders and insulin resistant diabetes)

RN 778576-81-1 CAPLUS
CN 1-Dibenzofurancarboxamide, 4-methoxy-8-nitro-N-(phenylmethyl)- (9CI) (CA INDEX NAME)



RN 778576-82-2 CAPLUS
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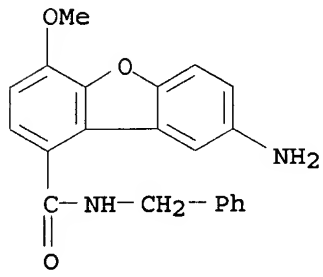


L6 ANSWER 3 OF 14 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2004:878393 CAPLUS
DOCUMENT NUMBER: 141:366121
TITLE: Preparation of dibenzo[b,f]furan-1-carboxamides, 9H-carbazole-4-carboxamides, and dibenzo[b,d]thiophene-4-carboxamides as PDE4 inhibitors for the treatment of

inflammatory and allergic disorders

INVENTOR(S): Gopalan, Balasubramanian; Gharat, Laxmikant Atmaram; Lakdawala, Aftab Dawoodbhai; Karaunakaran, Usha

PATENT ASSIGNEE(S): Glenmark Pharmaceuticals Ltd., India

SOURCE: PCT Int. Appl., 121 pp.
CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 2

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2004089940	A1	20041021	WO 2004-IB355	20040211
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: BW, GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
AU 2004228453	A1	20041021	AU 2004-228453	20040211
CA 2522023	AA	20041021	CA 2004-2522023	20040211
EP 1620429	A1	20060201	EP 2004-710093	20040211
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK				
BR 2004009747	A	20060509	BR 2004-9747	20040211
US 2005027129	A1	20050203	US 2004-821642	20040409
NO 2005005316	A	20060111	NO 2005-5316	20051110

PRIORITY APPLN. INFO.:

IN 2003-MU363	A	20030411
US 2003-519967P	P	20031113
WO 2004-IB355	W	20040211

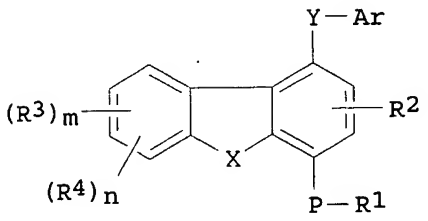
OTHER SOURCE(S): CASREACT 141:366121; MARPAT 141:366121

GI

issued application allowed

Not ODP

$-NH_2$.



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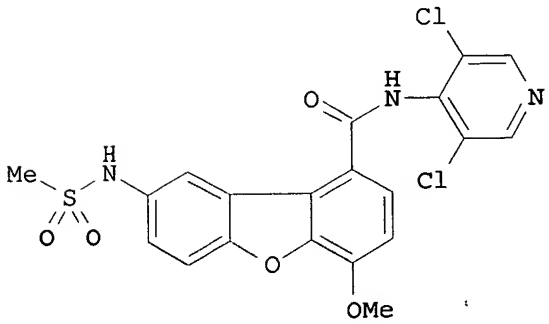


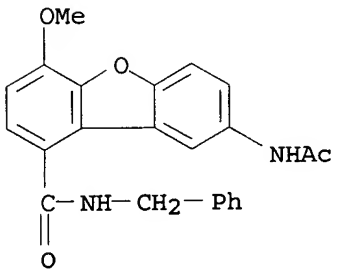
II

AB Title heterocyclic tricycles I [wherein R1-R3, R5, R6, Ra = independently H, (un)substituted (cyclo)alkyl, (cyclo)alkenyl, alkynyl, (hetero)aryl, heterocyclyl(alkyl), etc.; R4 = NR5R6, heterocyclyl; Ar = (un)substituted aryl(alkyl), heterocyclyl, heteroaryl; X = O, SO0-2, NRa; Y = CONR7, NR7SO0-2, SO0-2NR7, NR7CO; R7 = H, OH, ORa, (un)substituted alkyl, aryl, heterocyclyl; P = O, S; m = 0-3; n = 1-4; and tautomers, regioisomers, stereoisomers, enantiomers, diastereomers, polymorphs, N-oxides, pharmaceutically acceptable salts, solvates, and compns. thereof] were prepd. as phosphodiesterase type 4 (PDE4) inhibitors. For example, N-(3,5-dichloropyrid-4-yl)-4-methoxy-8-aminodibenzo[b,f]furan-1-carboxamide (prepd. in six steps from isovanillin, 4-fluoronitrobenzene, and 4-amino-3,5-dichloropyridine) was coupled with methanesulfonyl chloride in THF and pyridine to give the sulfonamide II. The latter inhibited the PDE4-induced conversion of [3H] cAMP to the corresponding [3H] 5'-AMP with IC50 of 0.5058 nM. Thus, I and their pharmaceutical compns. are useful for the treatment of immune disorders, inflammatory conditions, allergic conditions, CNS diseases, and insulin resistant diabetes (no data).

IT 778576-80-0P, N-Benzyl-4-methoxy-8-acetamidodibenzo[b,d]furan-1-carboxamide
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(PDE4 inhibitor; prepn. of tricyclic heterocycles as PDE4 inhibitors for treatment of immune and inflammatory disorders and insulin resistant diabetes)

RN 778576-80-0 CAPLUS

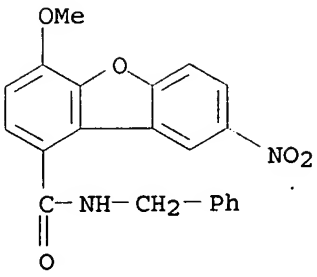
CN 1-Dibenzofurancarboxamide, 8-(acetylamino)-4-methoxy-N-(phenylmethyl)- (9CI) (CA INDEX NAME)



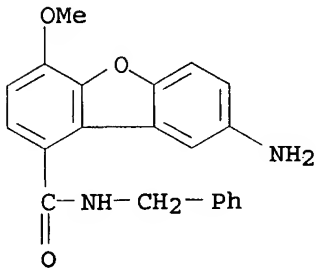
IT 778576-81-1P, N-Benzyl-4-methoxy-8-nitrodibenzo[b,d]furan-1-carboxamide 778576-82-2P, N-Benzyl-4-methoxy-8-aminodibenzo[b,d]furan-1-carboxamide
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(intermediate; prepn. of tricyclic heterocycles as PDE4 inhibitors for treatment of immune and inflammatory disorders and insulin resistant diabetes)

RN 778576-81-1 CAPLUS

CN 1-Dibenzofurancarboxamide, 4-methoxy-8-nitro-N-(phenylmethyl)- (9CI) (CA INDEX NAME)



RN 778576-82-2 CAPLUS
CN 1-Dibenzofurancarboxamide, 8-amino-4-methoxy-N-(phenylmethyl)- (9CI) (CA INDEX NAME)



REFERENCE COUNT: 6 THERE ARE 6 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L6 ANSWER 4 OF 14 CAPLUS COPYRIGHT 2006 ACS on STN Current application

ACCESSION NUMBER: 2004:370918 CAPLUS
DOCUMENT NUMBER: 140:391192
TITLE: Preparation of dibenzofuran/dibenzothiophene derivatives useful for the treatment of inflammatory and allergic disorders
INVENTOR(S): Balasubramanian, Gopalan; Gharat, Laxmikant Atmaram; Lakdawala, Aftab Dawoodbhai; Anupindi, Raghu Ram
PATENT ASSIGNEE(S): Glenmark Pharmaceuticals Ltd., India
SOURCE: PCT Int. Appl., 254 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

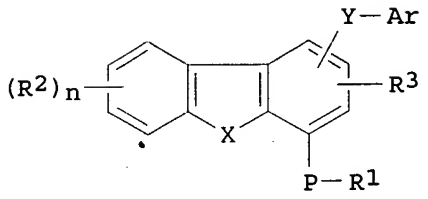
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2004037805	A1	20040506	WO 2003-IB4442	20031008
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
CA 2503015	AA	20040506	CA 2003-2503015	20031008
AU 2003269317	A1	20040513	AU 2003-269317	20031008
EP 1554262	A1	20050720	EP 2003-751096	20031008

R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK

BR 2003014721	A	20050802	BR 2003-14721		20031008
CN 1729181	A	20060201	CN 2003-80107246		20031008
JP 2006506379	T2	20060223	JP 2004-546246		20031008
US 2006178418	A1	20060810	US 2005-532273		20050926
PRIORITY APPLN. INFO.:			IN 2002-MU922	A	20021023
			WO 2003-IB4442	W	20031008

OTHER SOURCE(S): MARPAT 140:391192

GI



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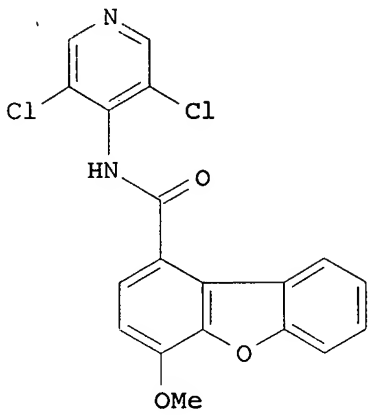


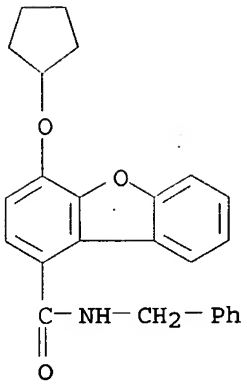
II

AB Title compds. I [R1-3 = H, alk(en/yn)yl, cycloalkyl, etc.; P = O, S; n = 0-4; Ar = (un)substituted aryl, etc.; Y = carboxamido, aminosulfonyl, etc.] are prepd. For instance, 4-methoxydibenzofuran-1-carboxylic acid (prepn. given) is converted to the corresponding acid chloride (PhH, SOCl2, reflux, 4 h) and treated with 4-amino-3,5-dichloropyridine (DMF/THF, NaH, -10.degree.) to give II. II has IC50 = 0.8 nM for PDE4. I are useful for the treatment of inflammatory conditions, diseases of the central nervous and insulin resistant diabetes.

IT 685875-05-2P, N-Benzyl-4-cyclopentyloxydibenzofuran-1-carboxamide
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(prepn. of dibenzofuran/dibenzothiophene derivs. useful for treatment of inflammatory and allergic disorders)

RN 685875-05-2 CAPLUS

CN 1-Dibenzofurancarboxamide, 4-(cyclopentyloxy)-N-(phenylmethyl)- (9CI) (CA INDEX NAME)



L6 ANSWER 5 OF 14 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1999:582679 CAPLUS
DOCUMENT NUMBER: 131:214557
TITLE: Preparation of N-Bpoc amino acid pentafluorophenyl (Pfp) esters and 3,4-dihydro-4-oxo-1,2,3-benzotriazin-3-yl (ODhbt) esters
INVENTOR(S): Carey, Robert I.
PATENT ASSIGNEE(S): University of Georgia Research Foundation, USA
SOURCE: U.S., 16 pp.
CODEN: USXXAM
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.		DATE
US 5952497	A	19990914	US 1997-891676		19970710
PRIORITY APPLN. INFO.:			US 1996-21499P	P	19960710

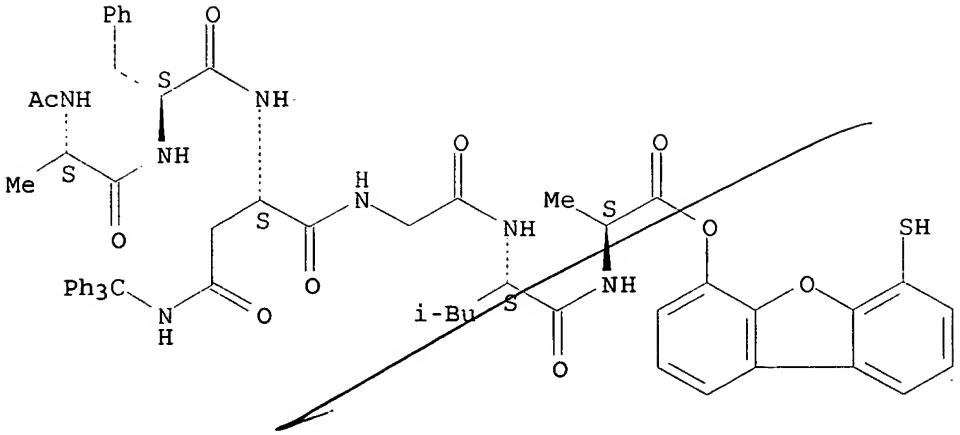
OTHER SOURCE(S): MARPAT 131:214557

AB Bpoc-Xxx-OPfp and Bpoc-Xxx-ODhbt [Bpoc = 2-(p-biphenyl)-2-propyloxycarbonyl, Xxx is an amino acid, Pfp = pentafluorophenyl, Dhbt = 3,4-dihydro-4-oxo-1,2,3-benzotriazin-3-yl] were prepd. for use in peptide synthesis. Thus, Bpoc-Phe-OPfp was prepd. from the acid by N-protection with Bpoc-OPh and esterification with pentafluorophenol and coupled with alanine Me ester to afford Bpoc-Phe-Ala-OMe.

IT 177609-17-5P 177609-18-6P
RL: SPN (Synthetic preparation); PREP (Preparation)
(prepn. of Bpoc amino acid pentafluorophenyl esters and dihydrooxobenzotriazinyl esters)

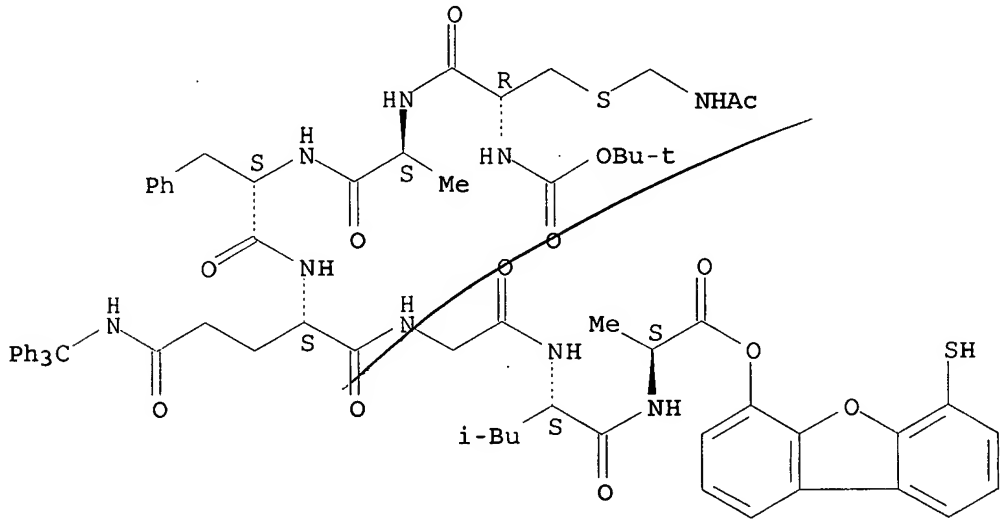
RN 177609-17-5 CAPLUS
CN Myotropic neuropeptide I (Leptinotarsa decemlineata), N-acetyl-2-L-phenylalanine-3-[N-(triphenylmethyl)-L-asparagine]-5-de-L-proline-7-L-alanine-, 6-mercapto-4-dibenzofuranyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 177609-18-6 CAPLUS
CN L-Alanine, N-[N-[N-[N2-[N-[N-[S-[(acetylamino)methyl]-N-[(1,1-dimethylethoxy)carbonyl]-L-cysteinyl]-L-alanyl]-L-phenylalanyl]-N-(triphenylmethyl)-L-glutaminyl]glycyl]-L-leucyl]-, 6-mercapto-4-dibenzofuranyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.



REFERENCE COUNT: 55 THERE ARE 55 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L6 ANSWER 6 OF 14 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1996:257151 CAPLUS
DOCUMENT NUMBER: 125:34137
TITLE: Protection of asparagine and glutamine during N.alpha.-Bpoc-based solid-phase peptide synthesis
AUTHOR(S): Carey, Robert I.; Huang, Haihong; Wadsworth, James L.; Burrell, C. Scott
CORPORATE SOURCE: Center Metalloenzyme Studies, Univ. Georgia, Athens, GA, 30602, USA
SOURCE: International Journal of Peptide & Protein Research (1996), 47(3), 209-13
CODEN: IJPPC3; ISSN: 0367-8377
PUBLISHER: Munksgaard
DOCUMENT TYPE: Journal
LANGUAGE: English
OTHER SOURCE(S): CASREACT 125:34137

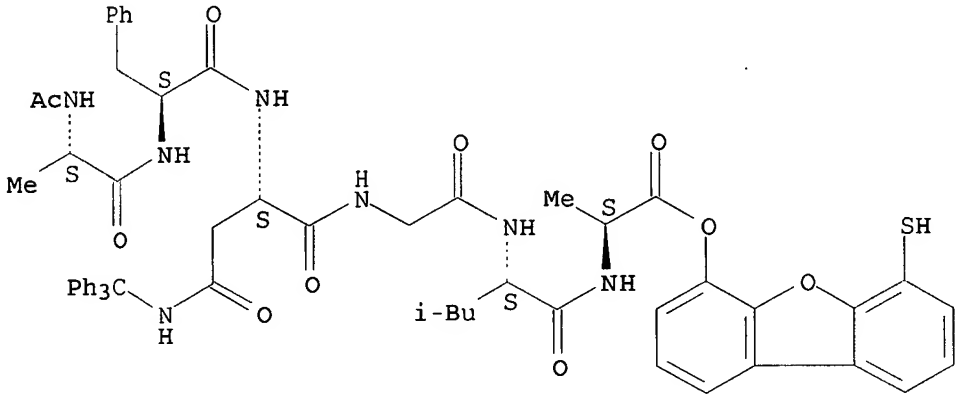
AB The synthesis and properties of title compds. Bpoc-Asn(Trt)-OPfp (Bpoc = 4-PhC6H4CMe2O2C; Trt = CPh3; Pfp = C6F5), Bpoc-Asn(Trt)-OH, Bpoc-Gln(Trt)-OPfp, and Bpoc-Gln(Trt)-OH are described. These derivs. are highly sol. in CH2Cl and can be coupled efficiently in solid-phase peptide synthesis. The peptides Ac-Ala-Phe-Asn(Trt)-Gly-Leu-Ala-O-Dbf-SH and Boc-Cys(Acm)-Ala-Phe-Gln(Trt)-Gly-Leu-Ala-O-Dbf-SH (HO-Dbf-SH = 4-mercapto-6-hydroxydibenzofuran) were synthesized by stepwise solid-phase peptide synthesis using N.alpha.-Bpoc amino acids. Less than 0.1% of the trityl group is removed from the Gln and Asn side chain during a std. 15 min N.alpha.-Bpoc deprotection in 0.5% TFA in CH2Cl2.

IT 177609-17-5P 177609-18-6P
RL: SPN (Synthetic preparation); PREP (Preparation)
(solid-phase synthesis of asparagine- and glutamine-contg. peptides using biphenylylisopropoxycarbonyl protective groups)

RN 177609-17-5 CAPLUS

CN Myotropic neuropeptide I (Leptinotarsa decemlineata), N-acetyl-2-L-phenylalanine-3-[N-(triphenylmethyl)-L-asparagine]-5-de-L-proline-7-L-alanine-, 6-mercapto-4-dibenzofuranyl ester (9CI) (CA INDEX NAME)

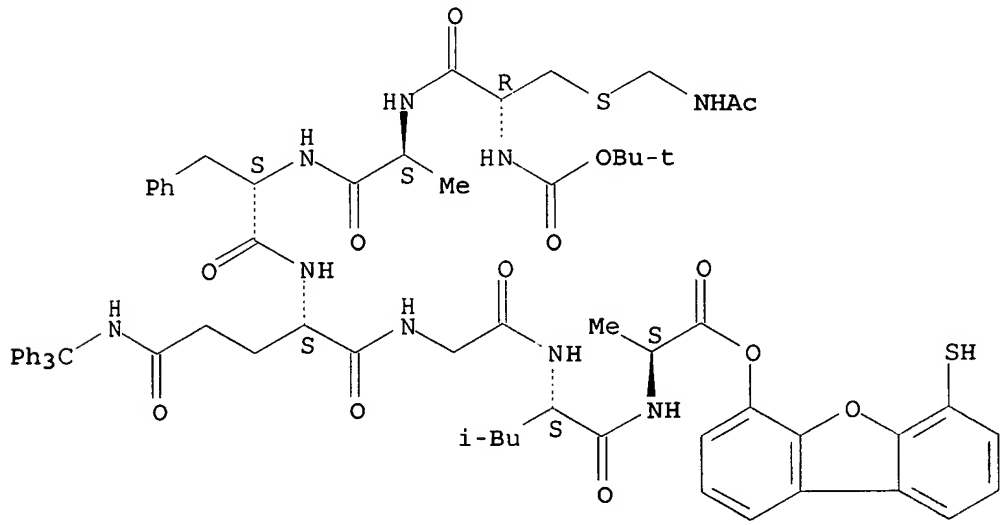
Absolute stereochemistry.



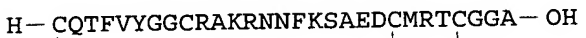
RN 177609-18-6 CAPLUS

CN L-Alanine, N-[N-[N-[N2-[N-[N-[S-[(acetylamino)methyl]-N-[(1,1-dimethylethoxy)carbonyl]-L-cysteinyl]-L-alanyl]-L-phenylalanyl]-N-(triphenylmethyl)-L-glutaminyl]glycyl]-L-leucyl]-, 6-mercapto-4-dibenzofuranyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L6 ANSWER 7 OF 14 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1993:473056 CAPLUS
DOCUMENT NUMBER: 119:73056
TITLE: Novel class of silicon-based protective groups for the side chain of tyrosine
AUTHOR(S): Fotouhi, Nader; Kemp, Daniel S.
CORPORATE SOURCE: Massachusetts Inst. Technol., Cambridge, MA, USA
SOURCE: International Journal of Peptide & Protein Research (1993), 41(2), 153-61
CODEN: IJPPC3; ISSN: 0367-8377
DOCUMENT TYPE: Journal
LANGUAGE: English
OTHER SOURCE(S): CASREACT 119:73056
GI



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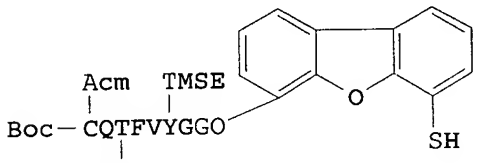


II

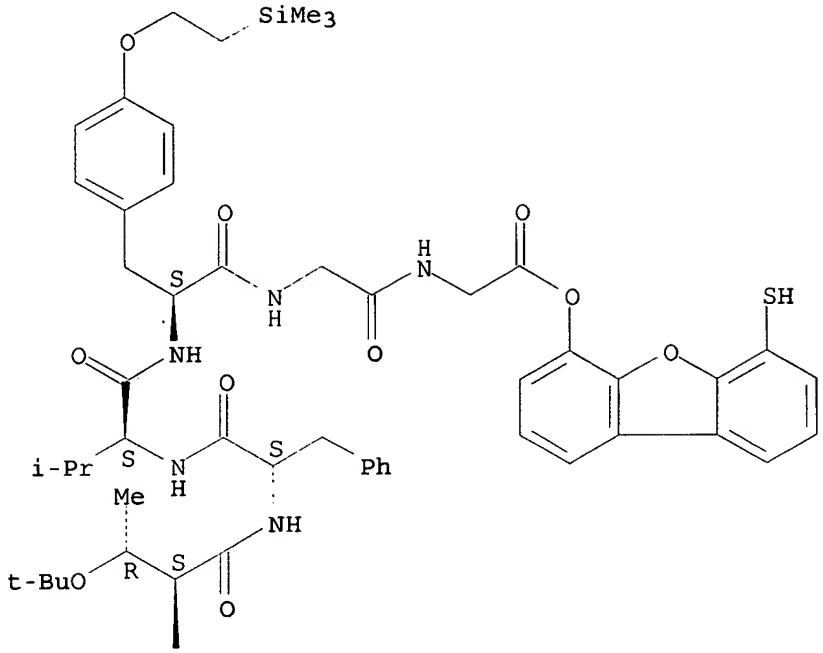
AB A novel class of silyl-based protective groups compatible with the biphenylisopropyloxycarbonyl (Bpoc)/tert-Bu strategy has been developed for the side chain of tyrosine. O-silyl-protected tyrosines Cbz-Tyr(TMSE)-OPNB [Cbz = carbobenzyloxy, TMSE = .beta.-(trimethylsilyl)ethyl, PNB p-nitrobenzyl], Bpoc-Tyr(TMSE)-OH.CHA (CHA = cyclohexylamine), and Cbz-Tyr(DMPSE)-OPNB [DMPSE = .beta.-(dimethylphenylsilyl)ethyl] were prepd. in reasonable yields and in very high purity. The TMSE group proved to be 3-4 times more stable than the tert-Bu ether group towards 0.5% TFA. The latter is removed up to 4% during the acidolysis of the Bpoc group. As expected, the DMPSE group was even more resistant towards 0.5% TFA (five time greater than the TMSE analog). Both silyl protective groups were found to be resistant towards a variety of reagents used in peptide synthesis, such as trialkylamines, hydroxybenzotriazole, trialkylphosphine and nucleophiles. They are readily removed in neat TFA in 5-20 min in the absence of cation scavengers, without any detectable alkylation of the phenolic ring. The application of the new silyl-based protective group was demonstrated by the synthesis of the C-terminal 29 amino acid peptide I (Acm = acetamidomethyl, Dnp = dinitrophenyl) of the basic pancreatic trypsin inhibitor by the prior thiol capture methodol. Protected octapeptide II (Boc = tert-butoxycarbonyl) was synthesized by solid-phase peptide synthesis using Bpoc-Tyr(TMSE)-OH in greater than 90% yield and coupled to an unprotected 21-mer. The partially blocked, purified peptide was deprotected quant. in neat TFA in 1 h.

IT 148982-18-7P 149002-20-0P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(prepn. and peptide coupling of, via thiol capture method)

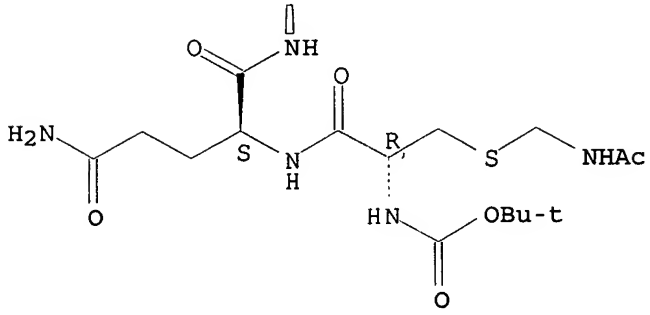
RN 148982-18-7 CAPLUS
CN Glycine, N-[N-[N-[N-[N-[N-[N2-[S-[(acetylamino)methyl]-N-[(1,1-dimethylethoxy)carbonyl]-L-cysteinyl]-L-glutaminyl]-O-(1,1-dimethylethyl)-L-threonyl]-L-phenylalanyl]-L-valyl]-O-[2-(trimethylsilyl)ethyl]-L-tyrosyl]glycyl]-, 6-mercapto-4-dibenzofuranyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



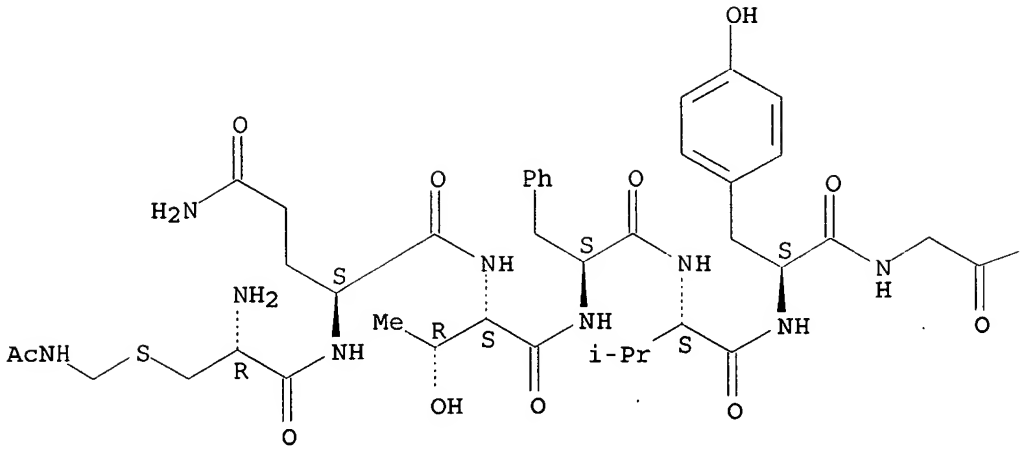
PAGE 2-A



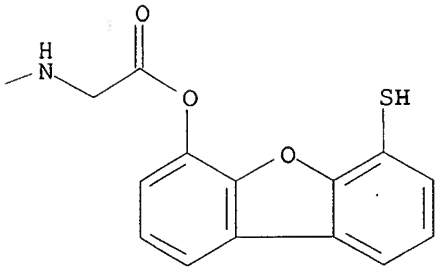
RN 149002-20-0 CAPLUS
CN Glycine, N-[N-[N-[N-[N-[N2-[S-[(acetylamino)methyl]-L-cysteinyl]-L-glutaminyl]-L-threonyl]-L-phenylalanyl]-L-valyl]-L-tyrosyl]glycyl]-, 6-mercapto-4-dibenzofuranyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



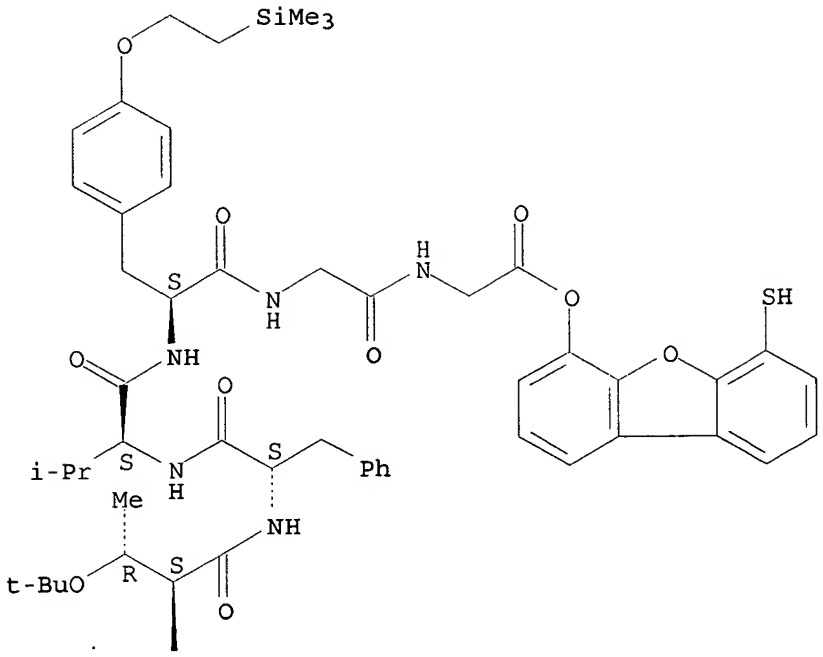
PAGE 1-B



IT 148982-18-7DP, resin-bound
RL: SPN (Synthetic preparation); PREP (Preparation)
(prepn. and resin cleavage of)
RN 148982-18-7 CAPLUS
CN Glycine, N-[N-[N-[N-[N-[N2-[S-[(acetylamino)methyl]-N-[(1,1-dimethylethoxy)carbonyl]-L-cysteinyl]-L-glutaminyl]-O-(1,1-dimethylethyl)-L-threonyl]-L-phenylalanyl]-L-valyl]-O-[2-(trimethylsilyl)ethyl]-L-tyrosyl]glycyl]-, 6-mercapto-4-dibenzofuranyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



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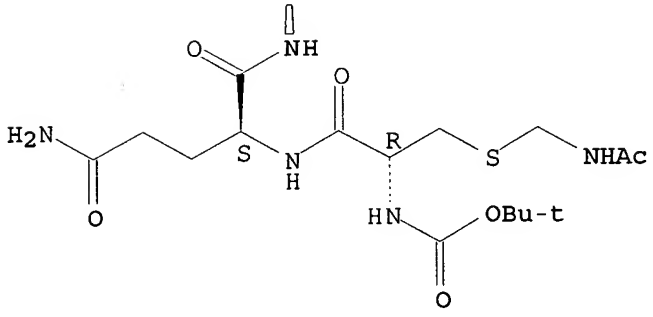


L6 ANSWER 8 OF 14 CAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 1993:234446 CAPLUS

DOCUMENT NUMBER: 118:234446

TITLE: Synthesis of a 39-peptide and a 25-peptide by thiol capture ligations: observation of a 40-fold rate acceleration of the intramolecular O,N-acyl-transfer reaction between peptide fragments bearing only cysteine protective groups

AUTHOR(S): Kemp, D. S.; Carey, Robert I.

CORPORATE SOURCE: Dep. Chem., Massachusetts Inst. Technol., Cambridge, MA, 02139, USA

SOURCE: Journal of Organic Chemistry (1993), 58(8), 2216-22
CODEN: JOCEAH; ISSN: 0022-3263

DOCUMENT TYPE: Journal

LANGUAGE: English

AB The syntheses of the 39-peptide H-Cys(Acm)Leu-Asn-Glu-Leu-Asp-Ala-Asp-Glu-Gln-Ala-Asp-Leu-Cys-Glu-Ser-Leu-His-Asp-His-Ala-Asp-Glu-Leu-Tyr-Arg-Ser-Cys-Leu-Ala-Arg-Phe-Gly-Asp-Asp-Gly-Glu-Asn-Leu-OH, and the 25-peptide H-Cys(Acm)Leu-Asn-Glu-Leu-Asp-Ala-Asp-Glu-Gln-Ala-Asp-Leu-Cys-Leu-Ala-Arg-

Phe-Gly-Asp-Asp-Gly-Glu-Asn-Leu-OH (I), via thiol capture ligations using precursor peptides bearing blocking groups only on cysteine residues is reported. The ligations were made in each case at the italicized Cys, cleanly and in high yield. For each of the above syntheses, an acidolytically deblocked 13-peptide dibenzofuranyl ester, 6-[H-Cys(Acm)Leu-Asn-Glu-Leu-Asp-Ala-Asp-Glu-Gln-Ala-Asp-Leu-O]-4-mercaptodibenzofuran, was prepd. in pure form in 52% overall yield through three stages: (1) stepwise synthesis on a solid-phase resin loaded with the dibenzofuran template, (2) acidolytic removal of the tert-Bu esters of the resin-bound peptide, and (3) preparative cleavage of the deblocked peptidyloxydibenzofuran ester from the resin. In the case of both the 39-peptide and the 25-peptide, significant rate enhancements were seen for the O,N-acyl transfer step of the thiol capture sequence when both the N-terminal and C-terminal fragments had been previously side-chain deblocked, in comparison with the cases when only the C-terminal fragment had been side chain deblocked. In the 13-peptide + 12-peptide ligation to form the 25-peptide I, a t1/2 = 5 min was seen for the leucine-cysteine amide bond forming reaction. A model leucine-cysteine O,N-acyl transfer as well as leucine-cysteine O,N-acyl transfers between protected peptide fragments, however, showed the expected t1/2 = 4 h. Rationalization of this obsd. 40-fold rate enhancement is offered that identifies the aspartic acid side chain carboxylate, 12 residues in sequence from the N-terminus and penultimate to the amide ligation site, as a possible intramol. general base catalyst for the proton transfer step during the O,N-acyl transfer.

IT 145618-25-3P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(prepn. and intramol. O,N-acyl transfer reaction of, kinetics of)

RN 145618-25-3 CAPLUS

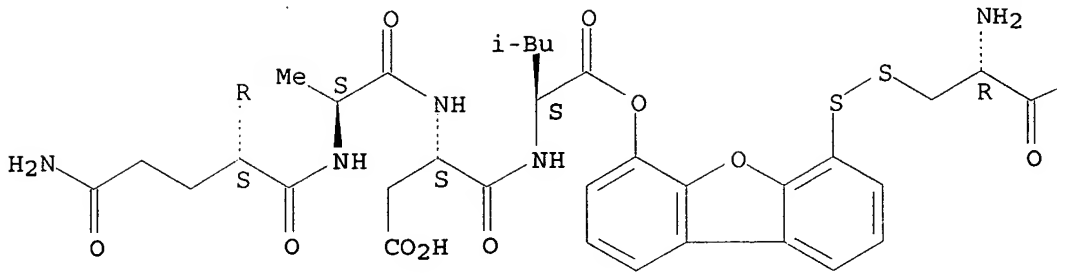
CN L-Leucine, N-[N2-[N-[N-[N-[N-[N-[N-[N2-[N-[N-[3-[[6-[[S-[(acetylamino)methyl]-L-cysteinyl-L-leucyl-L-asparaginyl-L-.alpha.-glutamyl-L-leucyl-L-.alpha.-aspartyl-L-alanyl-L-.alpha.-aspartyl-L-.alpha.-glutamyl-L-glutaminyl-L-alanyl-L-.alpha.-aspartyl-L-leucyl]oxy]-4-dibenzofuranyl]dithio]-L-alanyl]-L-leucyl]-L-alanyl]-L-arginyl]-L-phenylalanyl]glycyl]-L-.alpha.-aspartyl]-L-.alpha.-aspartyl]glycyl]-L-.alpha.-glutamyl]-L-asparaginyl]-, mono(trifluoroacetate) (9CI) (CA INDEX NAME)

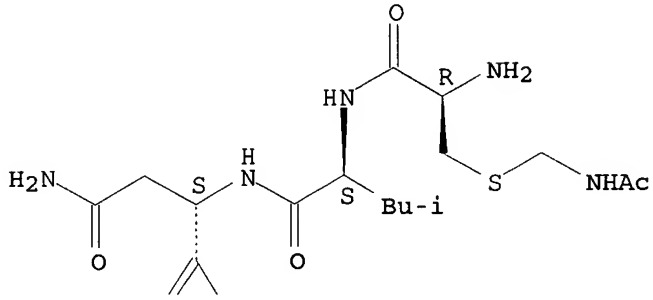
CM 1

CRN 145618-24-2
CMF C127 H186 N32 O48 S3

Absolute stereochemistry.

PAGE 1-A





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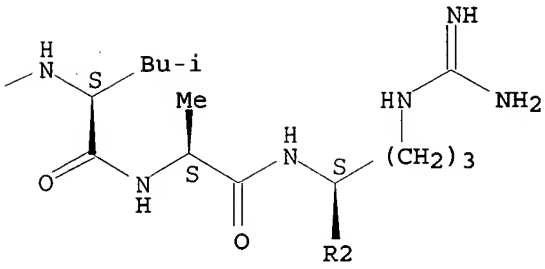

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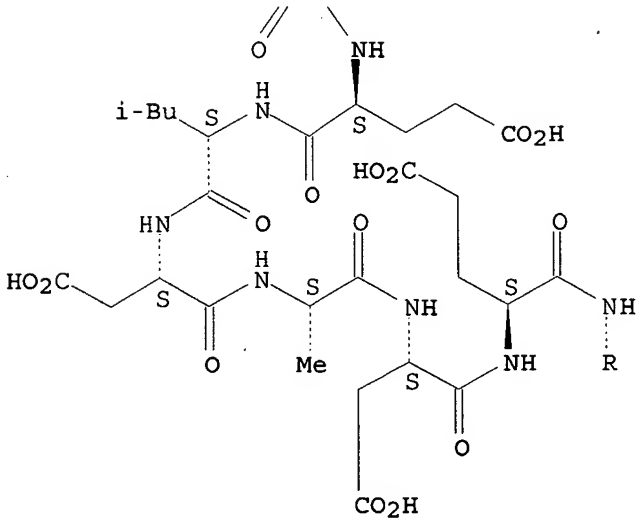
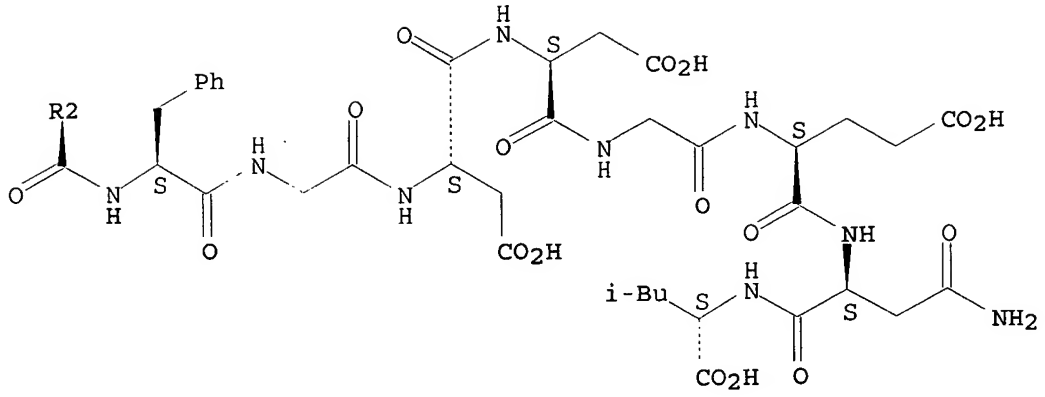
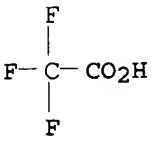


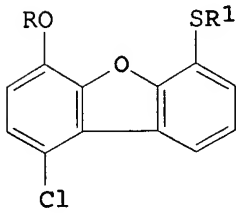


CM 2

CRN 76-05-1
CMF C2 H F3 O2



L6 ANSWER 9 OF 14 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1993:60085 CAPLUS
DOCUMENT NUMBER: 118:60085
TITLE: Resolution of proline acylation problem for thiol capture strategy by use of a chloro-dibenzofuran template
AUTHOR(S): Fotouhi, Nader; Bowen, Benjamin R.; Kemp, Daniel S.
CORPORATE SOURCE: Massachusetts Inst. Technol., Cambridge, MA, USA
SOURCE: International Journal of Peptide & Protein Research (1992), 40(2), 141-7
CODEN: IJPPC3; ISSN: 0367-8377
DOCUMENT TYPE: Journal
LANGUAGE: English
GI



I

AB The acyl transfer rate for proline, in the prior thiol capture strategy, was enhanced by changing the electronic character of the dibenzofuran template. The rate of amide bond formation between proline and cysteine by the 1-chloro-4-hydroxy-6-mercaptodibenzofuran template I [R = PhCH2O2C-Pro, R1 = L-H2NCH(CO2Me)CH2S] was 0.012 min-1, which translates to a half-life of 53 min. Further enhancement of the reaction rate was accomplished by the use of a 1,3-dichlorodibenzofuran template. The k1 for the reaction was 0.093 min-1, and the half-life was 7 min. To test the applicability of the activated template I (R = R1 = H) in peptide synthesis, a 34 amino acid peptide was synthesized. This peptide represents the condensation of the N-terminal 13-mer and the C-terminal 21-mer of the basic pancreatic trypsin inhibitor.

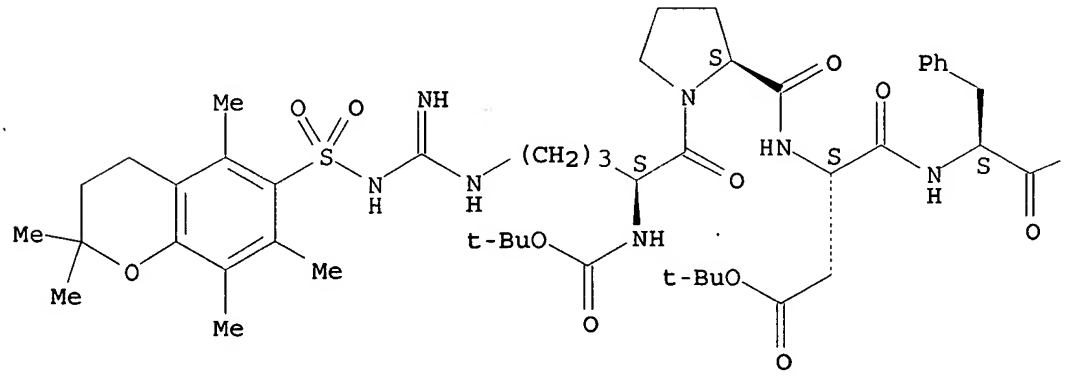
IT 145142-66-1P
RL: SPN (Synthetic preparation); PREP (Preparation)
(prepn. of, by solid-phase method and sequential disulfide coupling of, with cysteine-contg. peptide fragment, and intramol. peptide coupling of)

RN 145142-66-1 CAPLUS

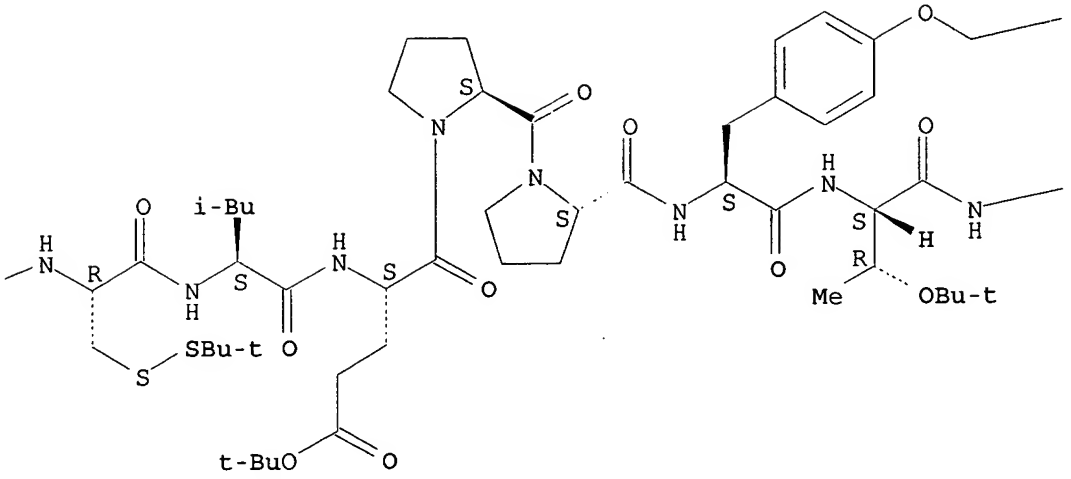
CN L-Proline, N5-[[[(3,4-dihydro-2,2,5,7,8-pentamethyl-2H-1-benzopyran-6-yl)sulfonyl]amino]iminomethyl]-N2-[(1,1-dimethylethoxy)carbonyl]-L-ornithyl-L-prolyl-L-.alpha.-aspartyl-L-phenylalanyl-3-[(1,1-dimethylethyl)dithio]-L-alanyl-L-leucyl-L-.alpha.-glutamyl-L-prolyl-L-prolyl-O-[2-(trimethylsilyl)ethyl]-L-tyrosyl-O-(1,1-dimethylethyl)-L-threonylglycyl-, 13-(1-chloro-6-mercapto-4-dibenzofuranyl) 3,7-bis(1,1-dimethylethyl) ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.

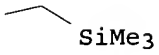
PAGE 1-A

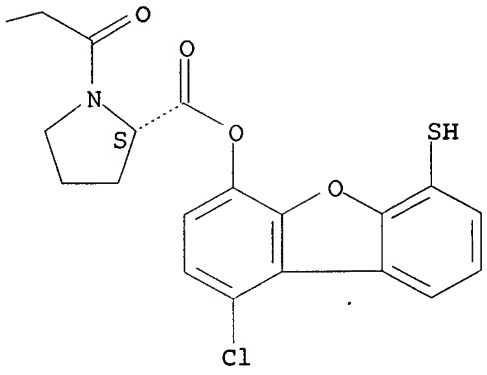


PAGE 1-B



PAGE 1-C





L6 ANSWER 10 OF 14 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1989:407776 CAPLUS
DOCUMENT NUMBER: 111:7776
TITLE: Peptide synthesis by prior thiol capture. 6. Rates of the disulfide-bond-forming capture reaction and demonstration of the overall strategy by synthesis of the C-terminal 29-peptide sequence of BPTI
AUTHOR(S): Fotouhi, Nader; Galakatos, Nicholas George; Kemp, D. S.
CORPORATE SOURCE: Dep. Chem., Massachusetts Inst. Technol., Cambridge, MA, 02139, USA
SOURCE: Journal of Organic Chemistry (1989), 54(12), 2803-17
CODEN: JOCEAH; ISSN: 0022-3263
DOCUMENT TYPE: Journal
LANGUAGE: English
OTHER SOURCE(S): CASREACT 111:7776
AB Peptide bond formation by prior thiol capture involves as a first step

formation of a disulfide bond between two S-functionalized peptide fragments, one bearing a 4-(acyloxy)-6-mercaptodibenzofuran at its C-terminus, the other bearing an S-activated cysteine residue at its N-terminus. The Scm (Scm = methoxycarbonylsulfenyl) procedure was used to generate disulfides by the reaction of arene thiols with Cys(Scm) derivs. Mixts. of hexafluoroisopropyl alc. (HFIP) with water and acetonitrile facilitate this reaction, which is markedly accelerated by traces of tertiary amines, by electron-withdrawing groups near the Scm function, and by an increase in the fraction of water in the mixt. The scope of the thiol capture strategy is demonstrated by a four-fragment, three-stage assembly of the 29-peptide sequence 30-58 of basic pancreatic trypsin inhibitor.

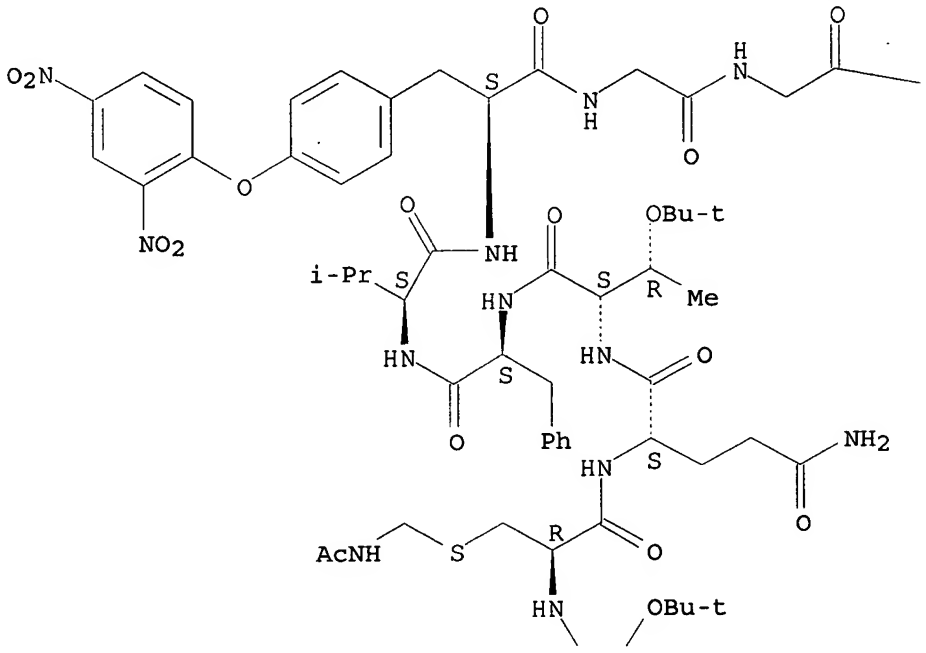
IT 120411-14-5P 120411-20-3P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(prepn. and disulfide coupling reaction of, with cysteine-contg. peptide)

RN 120411-14-5 CAPLUS

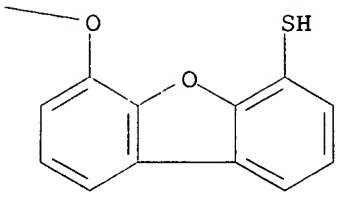
CN Glycine, N-[N-[N-[N-[N-[N2-[S-[(acetylamino)methyl]-N-[(1,1-dimethylethoxy)carbonyl]-L-cysteinyl]-L-glutaminyl]-O-(1,1-dimethylethyl)-L-threonyl]-L-phenylalanyl]-L-valyl]-O-(2,4-dinitrophenyl)-L-tyrosyl]glycyl]-, 6-mercapto-4-dibenzofuranyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



PAGE 1-B



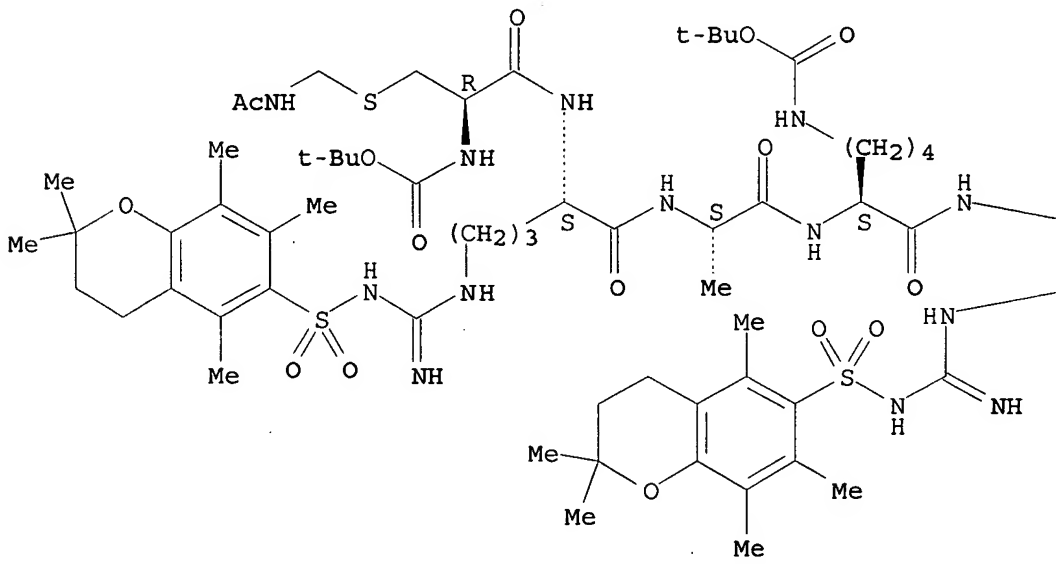
PAGE 2-A

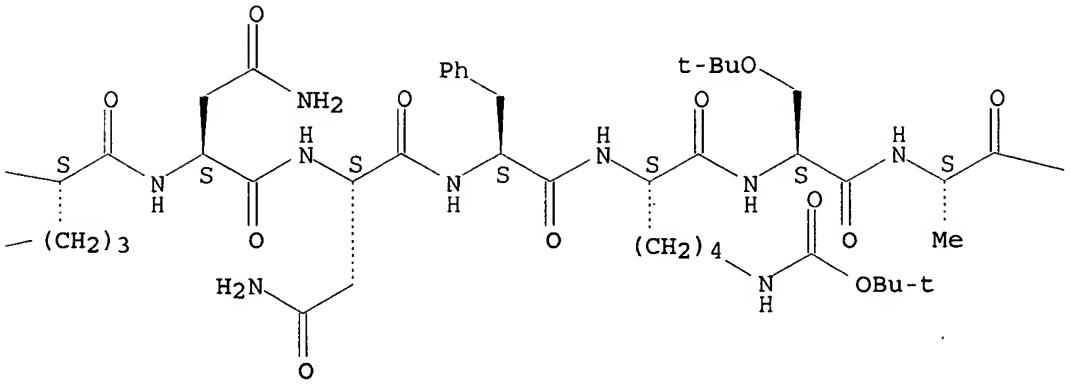
RN 120411-20-3 CAPLUS

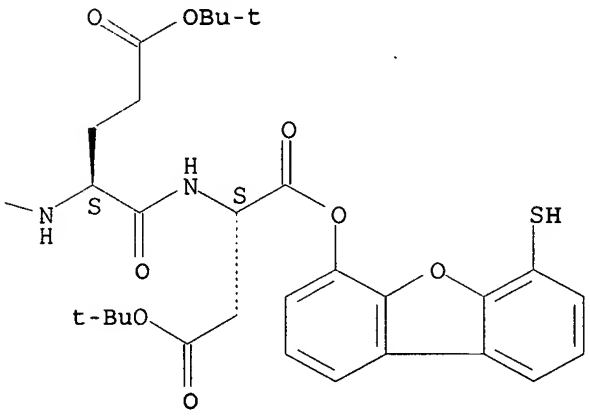
CN L-Aspartic acid, S-[(acetylamino)methyl]-N-[(1,1-dimethylethoxy)carbonyl]-L-cysteinyl-N5-[[[(3,4-dihydro-2,2,5,7,8-pentamethyl-2H-1-benzopyran-6-yl)sulfonyl]amino]iminomethyl]-L-ornithyl-L-alanyl-N6-[(1,1-dimethylethoxy)carbonyl]-L-lysyl-N5-[[[(3,4-dihydro-2,2,5,7,8-pentamethyl-2H-1-benzopyran-6-yl)sulfonyl]amino]iminomethyl]-L-ornithyl-L-asparaginyl-L-asparaginyl-L-phenylalanyl-N6-[(1,1-dimethylethoxy)carbonyl]-L-lysyl-O-(1,1-dimethylethyl)-L-seryl-L-alanyl-L-.alpha.-glutamyl-, 12,134-bis(1,1-dimethylethyl) 131-(6-mercapto-4-dibenzofuranyl) ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A







L6 ANSWER 11 OF 14 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1988:222109 CAPLUS
DOCUMENT NUMBER: 108:222109
TITLE: Peptide synthesis by prior thiol capture. V. Scope and control of disulfide interchange during the acyl-transfer step
AUTHOR(S): Kemp, D. S.; Fotouhi, Nader
CORPORATE SOURCE: Dep. Chem., Massachusetts Inst. Technol., Cambridge, MA, 02139, USA
SOURCE: Tetrahedron Letters (1987), 28(40), 4637-40
CODEN: TELEAY; ISSN: 0040-4039
DOCUMENT TYPE: Journal
LANGUAGE: English
OTHER SOURCE(S): CASREACT 108:222109

AB Disulfide interchange in DMSO during amide formation by prior thiol capture is reduced to less than 3% at low concns. (<10 M) of substrate in the absence of air and light, and in the presence of 2.5 to 10 mol % AgNO3. The rate and selectivity of the exchange process were assessed by reacting Me3CO2C-Cys(SR)-Ala-OCH2C6H4NO2-4 (I, R = 4-dibenzofuranyl) with a thiol. I (R = Ph or PhCH2) was formed almost exclusively.

IT 114518-93-3
RL: RCT (Reactant); RACT (Reactant or reagent)

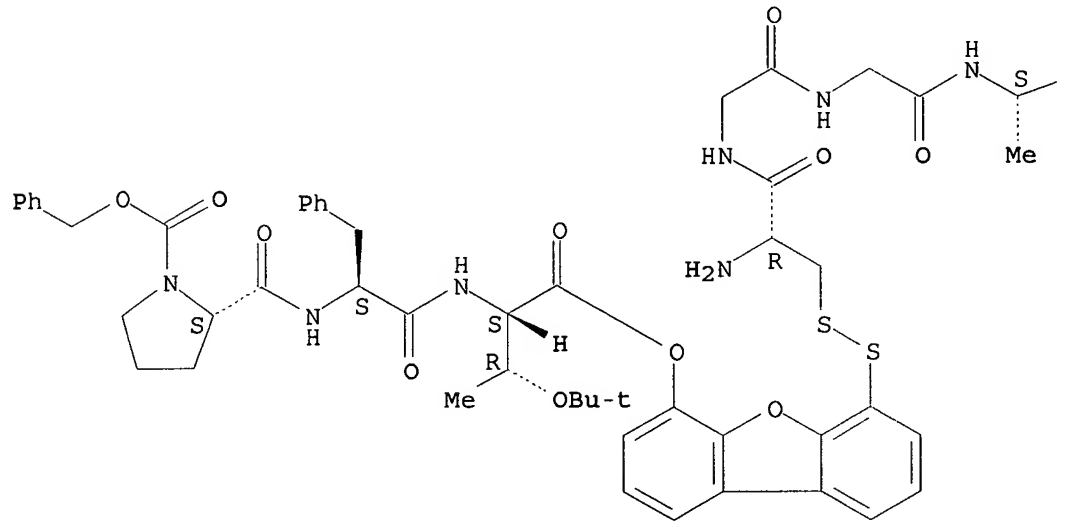
(intramol. peptide coupling of)

RN 114518-93-3 CAPLUS

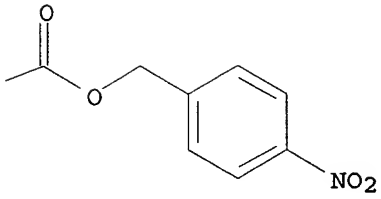
CN L-Alanine, N-[N-[N-[3-[(6-hydroxy-4-dibenzofuranyl)dithio]-L-alanyl]glycyl]glycyl]-, (4-nitrophenyl)methyl ester, ester with O-(1,1-dimethylethyl)-N-[N-[1-[(phenylmethoxy)carbonyl]-L-prolyl]-L-phenylalanyl]-L-threonine (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



PAGE 1-B



IT 114518-94-4P

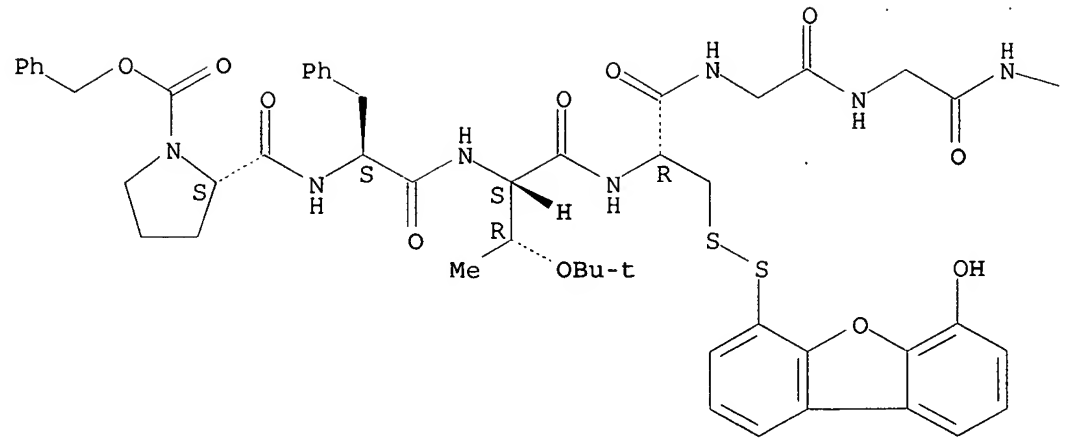
RL: SPN (Synthetic preparation); PREP (Preparation)
(prepn. of)

RN 114518-94-4 CAPLUS

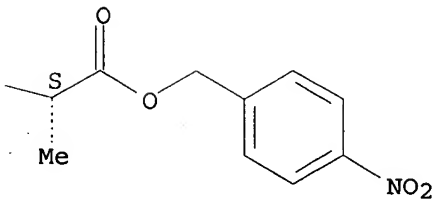
CN L-Alanine, N-[N-[N-[N-[O-(1,1-dimethylethyl)-N-[N-[1-[(phenylmethoxy)carbonyl]-L-prolyl]-L-phenylalanyl]-L-threonyl]-3-[(6-hydroxy-4-dibenzofuranyl)dithio]-L-alanyl]glycyl]glycyl]-, (4-nitrophenyl)methyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



PAGE 1-B



L6 ANSWER 12 OF 14 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1988:187255 CAPLUS
DOCUMENT NUMBER: 108:187255
TITLE: Peptide synthesis by prior thiol capture. III. Assessment of levels of racemization during two typical thiol capture coupling reactions
AUTHOR(S): McBride, Bill J.; Kemp, D. S.
CORPORATE SOURCE: Dep. Chem., Massachusetts Inst. Technol., Cambridge, MA, 02139, USA
SOURCE: Tetrahedron Letters (1987), 28(30), 3435-8
CODEN: TELEAY; ISSN: 0040-4039
DOCUMENT TYPE: Journal
LANGUAGE: English
OTHER SOURCE(S): CASREACT 108:187255

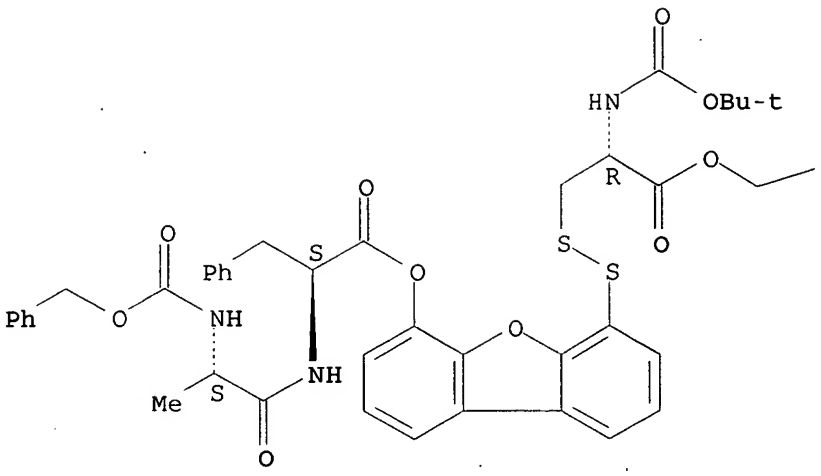
AB Racemization during peptide bond formation by the dibenzofuran-based thiol capture strategy has been assessed through synthesis of two model peptides, Z-L-Ala-L-Ile-Cys-OMe (Z = PhCH2O2C) and Z-L-Ala-L-Phe-L-Cys-OMaq (Maq = 2-oxymethylanthraquinone moiety). The former case gave (0.20 .+-. 0.27) % of the D-aIle epimer and the latter, less than 0.1% of the L-D-L-epimer.

IT 114208-45-6P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(prepn. and acyl transfer reaction of)

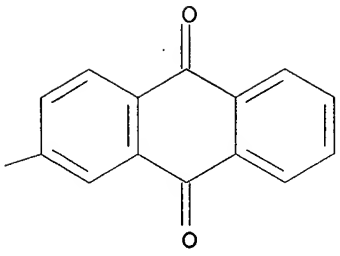
RN 114208-45-6 CAPLUS
CN L-Phenylalanine, N-[N-[(phenylmethoxy)carbonyl]-L-alanyl]-, ester with N-[(1,1-dimethylethoxy)carbonyl]-3-[(6-hydroxy-4-dibenzofuranyl)dithio]-L-alanine (9,10-dihydro-9,10-dioxo-2-anthracenyl)methyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A

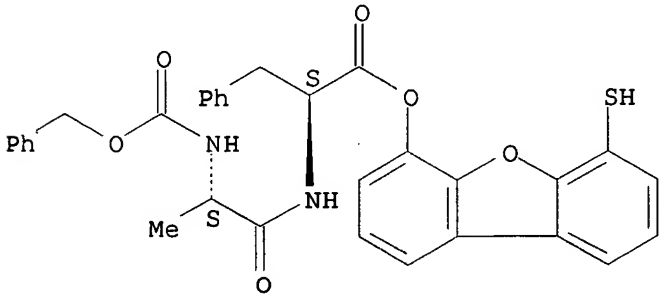


PAGE 1-B



IT 114208-44-5DP, disulfide with mercapto resin
RL: SPN (Synthetic preparation); PREP (Preparation)
(prepn. and disulfide cleavage and reaction with cystine deriv.)
RN 114208-44-5 CAPLUS
CN L-Phenylalanine, N-[N-[(phenylmethoxy)carbonyl]-L-alanyl]-, 6-mercapto-4-dibenzofuranyl ester (9CI) (CA INDEX NAME)

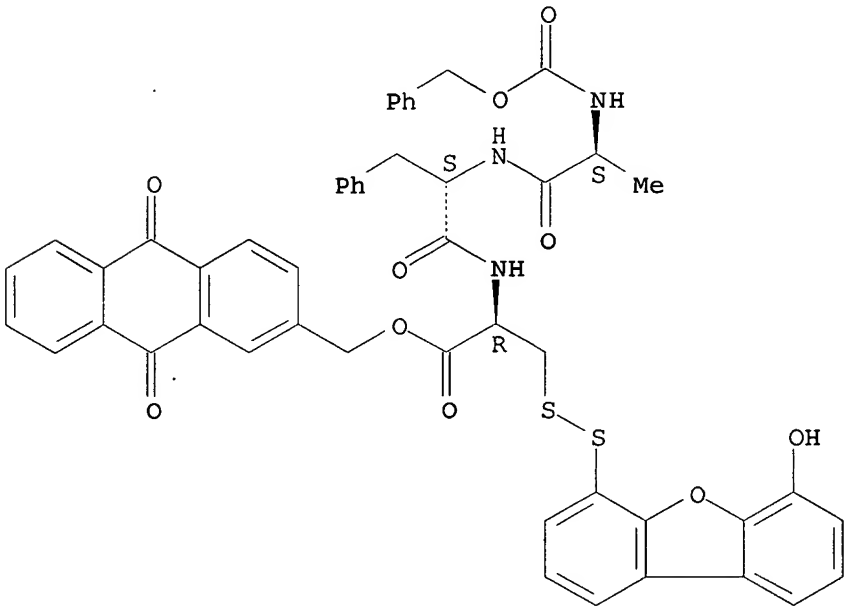
Absolute stereochemistry.



IT 114208-46-7P
RL: SPN (Synthetic preparation); PREP (Preparation)
(prepn. of, racemization in)
RN 114208-46-7 CAPLUS

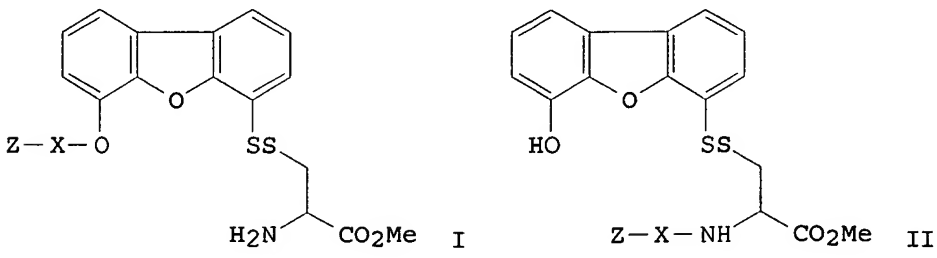
CN L-Alanine, 3-[(6-hydroxy-4-dibenzofuranyl)dithio]-N-[N-[N-[(phenylmethoxy)carbonyl]-L-alanyl]-L-phenylalanyl]-, (9,10-dihydro-9,10-dioxo-2-anthracenyl)methyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L6 ANSWER 13 OF 14 CAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 1986:515398 CAPLUS
DOCUMENT NUMBER: 105:115398
TITLE: Peptide synthesis by prior thiol capture. 4. Amide bond formation. The effect of a side-chain substituent on the rates of intramolecular O,N-acyl transfer
AUTHOR(S): Kemp, D. S.; Galakatos, Nicholas G.; Dranginis, Stanley; Ashton, Christopher; Fotouhi, Nader; Curran, Timothy P.
CORPORATE SOURCE: Dep. Chem., Massachusetts Inst. Technol., Cambridge, MA, 02139, USA
SOURCE: Journal of Organic Chemistry (1986), 51(17), 3320-4
CODEN: JOCEAH; ISSN: 0022-3263
DOCUMENT TYPE: Journal
LANGUAGE: English
OTHER SOURCE(S): CASREACT 105:115398
GI



AB The effects of varying steric bulk of the side chain substituent of the

acylating agent on the rate of the amide-bond forming step of the dibenzofuran-based thiol capture strategy were detd. from rates of intramol. O .fwdarw. N-acyl transfer of O-acyl dibenzofuran derivs. I [Z = PhCH2O2C; X = Ala, Leu, Pro, Val, Lys(Z), Asn, Asp, Arg(ans) (ans = 9-anthracenesulfonyl)] to the N-acyl derivs. II in DMSO at 25.degree.. Half times of 2-4 h were obsd. for all cases except for Pro and Val, which are roughly an order of magnitude slower, and for Asp, which shows evidence of intramol. general base catalysis by the neighboring carboxylate group. A steric rationalization for the anomalously slow proline transfer rate is proposed.

IT 103478-05-3
RL: RCT (Reactant); RACT (Reactant or reagent)
(intermol. O- .fwdarw. N-acyl transfer reaction of, kinetics of)

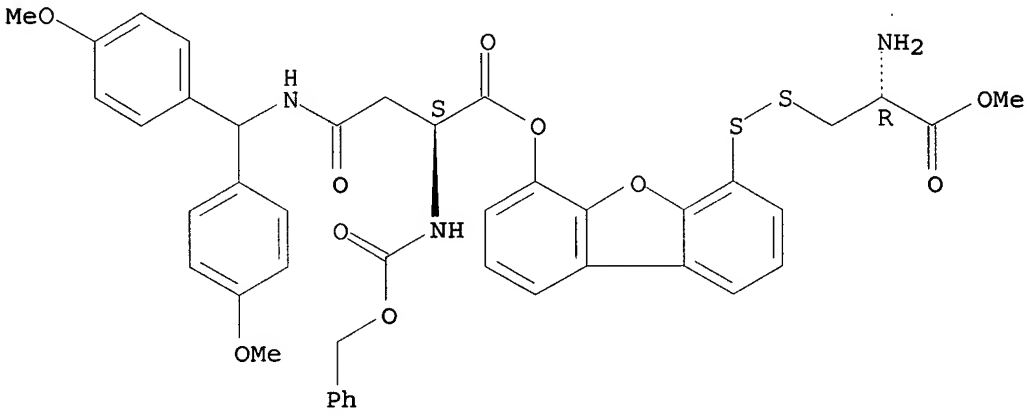
RN 103478-05-3 CAPLUS

CN L-Asparagine, N-[bis(4-methoxyphenyl)methyl]-N2-[(phenylmethoxy)carbonyl]-, ester with 3-[(6-hydroxy-4-dibenzofuranyl)dithio]-L-alanine methyl ester, mono(trifluoroacetate) (salt) (9CI) (CA INDEX NAME)

CM 1

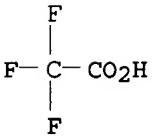
CRN 103478-04-2
CMF C43 H41 N3 O10 S2

Absolute stereochemistry.



CM 2

CRN 76-05-1
CMF C2 H F3 O2

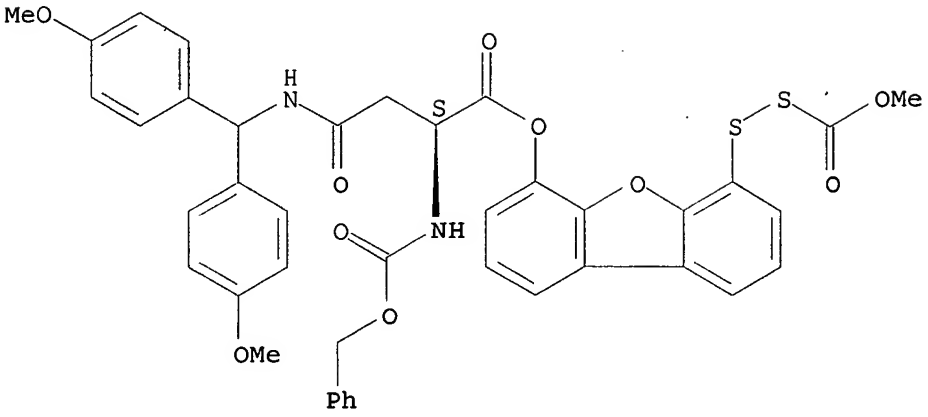


IT 103477-87-8P
RL: SPN (Synthetic preparation); PREP (Preparation)
(prepn. and partial deblocking of)

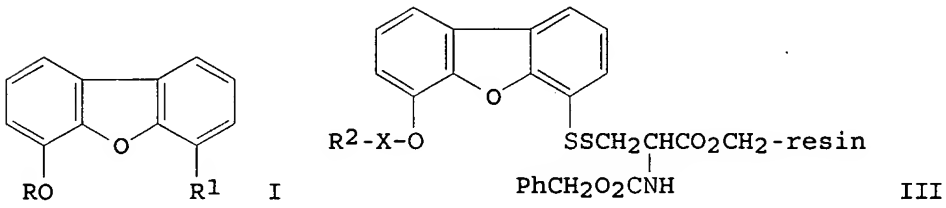
RN 103477-87-8 CAPLUS

CN L-Asparagine, N-[bis(4-methoxyphenyl)methyl]-N2-[(phenylmethoxy)carbonyl]-, 6-[(methoxycarbonyl)dithio]-4-dibenzofuranyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L6 ANSWER 14 OF 14 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1986:207668 CAPLUS
DOCUMENT NUMBER: 104:207668
TITLE: Peptide synthesis by prior thiol capture. 1. A convenient synthesis of 4-hydroxy-6-mercaptodibenzofuran and novel solid-phase synthesis of peptide-derived 4-(acyloxy)-6-mercaptodibenzofurans
AUTHOR(S): Kemp, D. S.; Galakatos, Nicholas George
CORPORATE SOURCE: Dep. Chem., Massachusetts Inst. Technol., Cambridge, MA, 02139, USA
SOURCE: Journal of Organic Chemistry (1986), 51(10), 1821-9
CODEN: JOCEAH; ISSN: 0022-3263
DOCUMENT TYPE: Journal
LANGUAGE: English
OTHER SOURCE(S): CASREACT 104:207668
GI



AB Benzoylfuran I (R = H, R1 = SH) (II) was prepd. as a template precursor for solid-phase peptide synthesis. Thus, II was obtained from I (R = Me, R1 = H) by metalation with BuLi, oxidn. with sulfur, and demethylation. O-Esters of II with N-protected amino acids were prepd. by direct O-acylation of I (R = H, R1 = SSCO2Me), followed by redn. with Bu3P. Resin-bound esters III (R2 = N-protective group, X = amino acid residue) were prepd. and used in solid-phase peptide synthesis in which chain elongation steps are carried out at the X residue. At the completion of the elongation steps, release of the peptide O-ester with II was achieved by redn. of the disulfide bond with Bu3P.

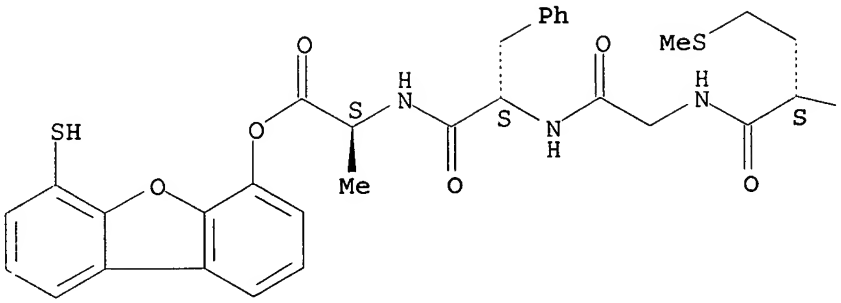
IT 101711-51-7P
RL: SPN (Synthetic preparation); PREP (Preparation)
(prepn. and disulfide reaction exchange reaction of, with cysteine deriv.)

RN 101711-51-7 CAPLUS
CN L-Alanine, N-[N-[N-[N-[(9H-fluoren-9-ylmethoxy)carbonyl]-L-

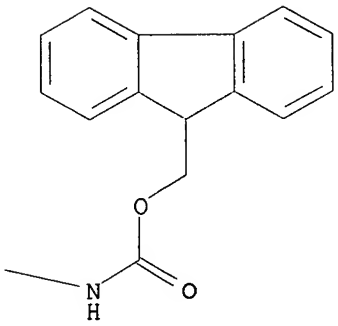
methionyl]glycyl]-L-phenylalanyl]-, 6-mercapto-4-dibenzofuranyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



PAGE 1-B



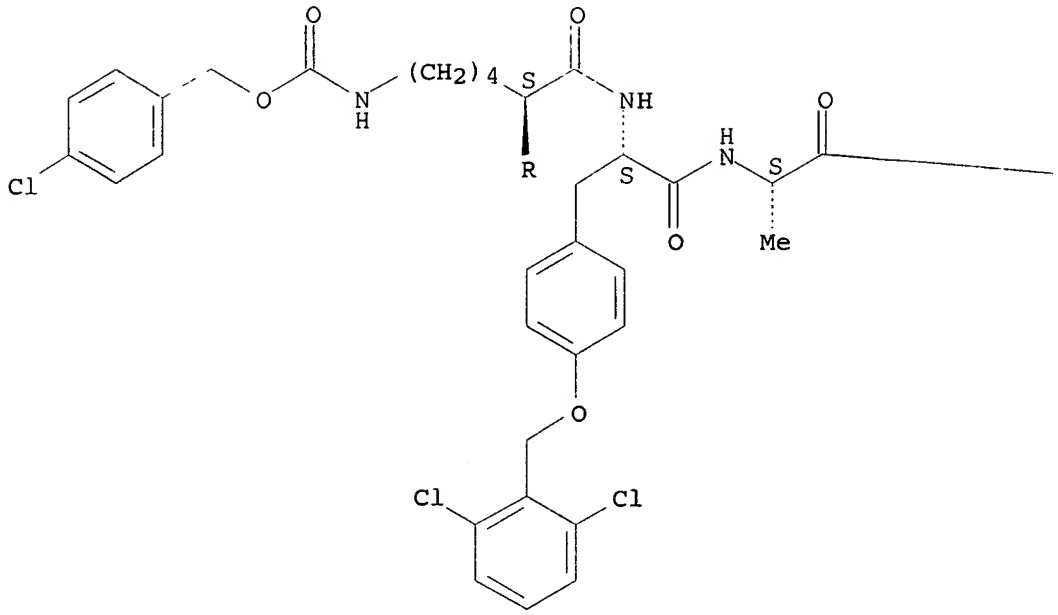
IT 101697-63-6DP, resin-bound
RL: SPN (Synthetic preparation); PREP (Preparation)
(prepn. and resin cleavage of)

RN 101697-63-6 CAPLUS

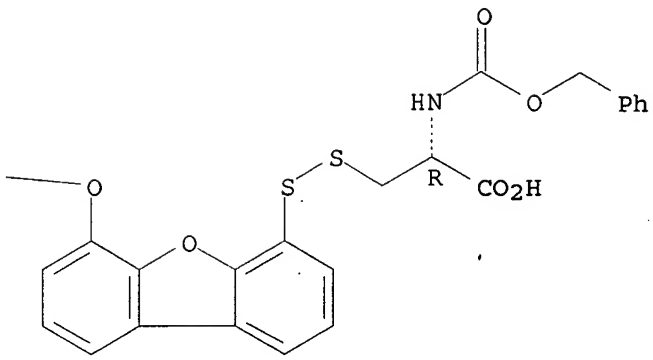
CN L-Alanine, N-[N-[N6-[[(4-chlorophenyl)methoxy]carbonyl]-N2-[N-[N-[N-[N-[N-[(phenylmethoxy)carbonyl]-L-isoleucyl]-L-.alpha.-glutamyl]-L-alanyl]-L-leucyl]-L-.alpha.-aspartyl]-L-lysyl]-O-[(2,6-dichlorophenyl)methyl]-L-tyrosyl]-, 4,5-bis(phenylmethyl) ester, 1-ester with 3-[(6-hydroxy-4-dibenzofuranyl)dithio]-N-[(phenylmethoxy)carbonyl]-L-alanine (9CI) (CA INDEX NAME)

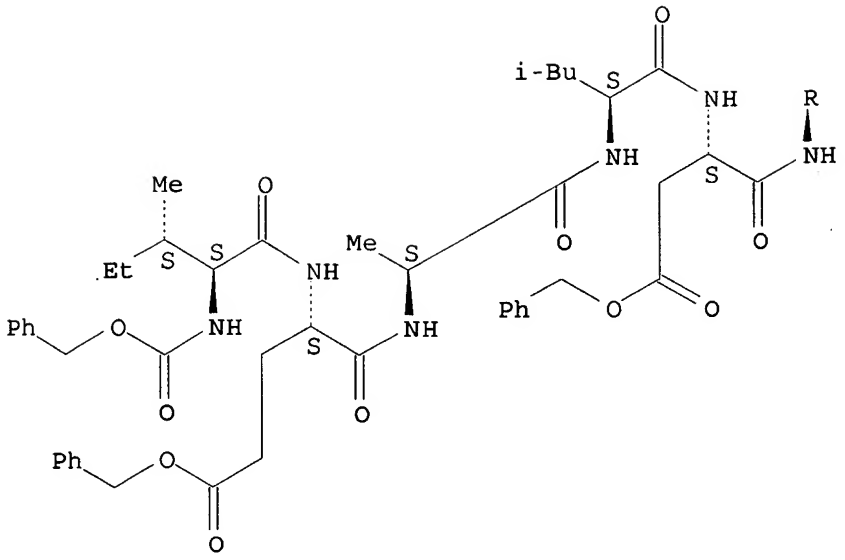
Absolute stereochemistry.

PAGE 1-A



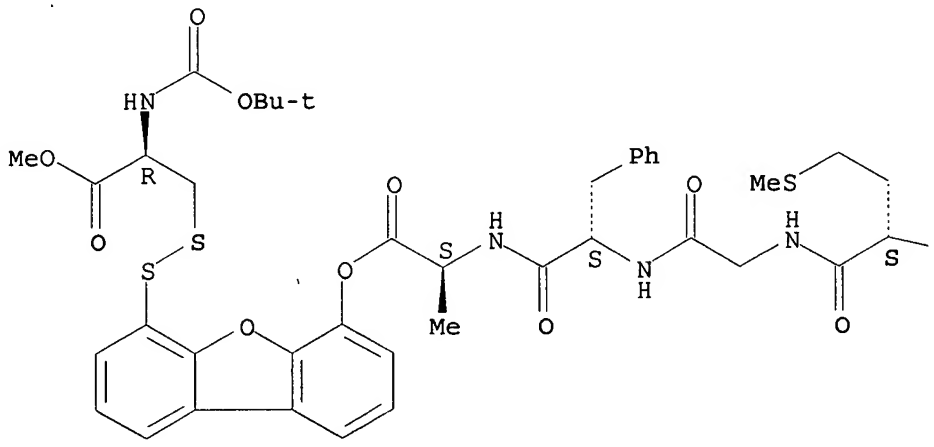
PAGE 1-B

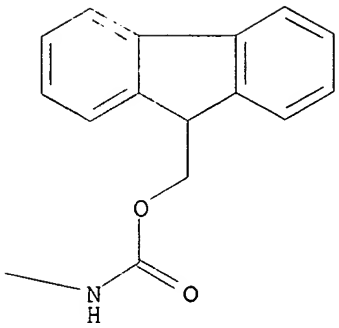




IT 101697-61-4P 101697-66-9P 101697-68-1P
101697-69-2P 101697-70-5P
RL: SPN (Synthetic preparation); PREP (Preparation)
(prepn. of)
RN 101697-61-4 CAPLUS
CN L-Alanine, N-[N-[N-[N-[(9H-fluoren-9-ylmethoxy)carbonyl]-L-methionyl]glycyl]-L-phenylalanyl]-, ester with N-[(1,1-dimethylethoxy)carbonyl]-3-[(6-hydroxy-4-dibenzofuranyl)dithio]-L-alanine methyl ester (9CI) (CA INDEX NAME)

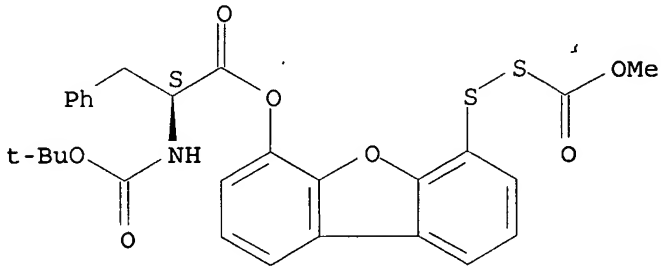
Absolute stereochemistry.





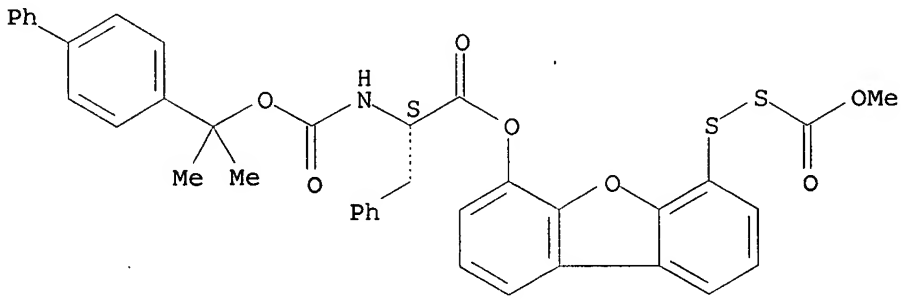
RN 101697-66-9 CAPLUS
CN L-Phenylalanine, N-[(1,1-dimethylethoxy)carbonyl]-, 6-[(methoxycarbonyl)dithio]-4-dibenzofuranyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.



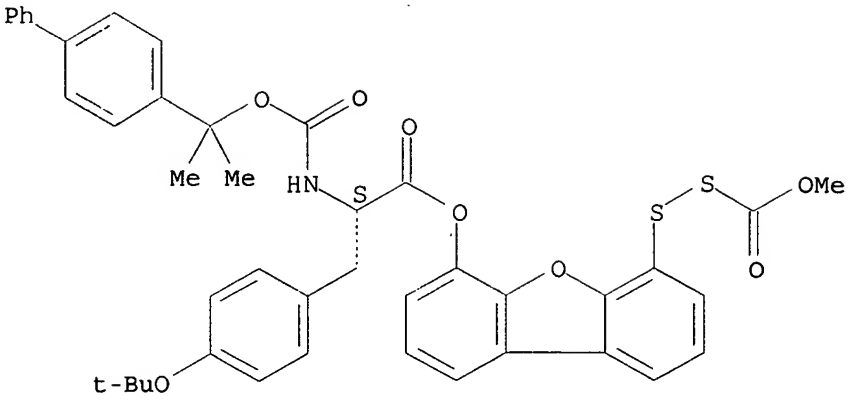
RN 101697-68-1 CAPLUS
CN L-Phenylalanine, N-[(1-[1,1'-biphenyl]-4-yl-1-methylethoxy)carbonyl]-, 6-[(methoxycarbonyl)dithio]-4-dibenzofuranyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.



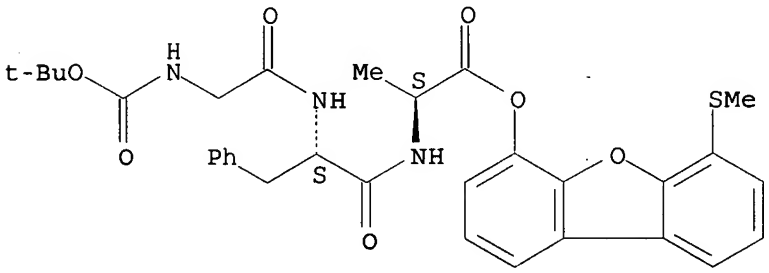
RN 101697-69-2 CAPLUS
CN L-Tyrosine, N-[(1-[1,1'-biphenyl]-4-yl-1-methylethoxy)carbonyl]-O-(1,1-dimethylethyl)-, 6-[(methoxycarbonyl)dithio]-4-dibenzofuranyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 101697-70-5 CAPLUS
CN L-Alanine, N-[N-[N-[(1,1-dimethylethoxy)carbonyl]glycyl]-L-phenylalanyl]-, 6-(methylthio)-4-dibenzofuranyl ester (9CI) (CA INDEX NAME)

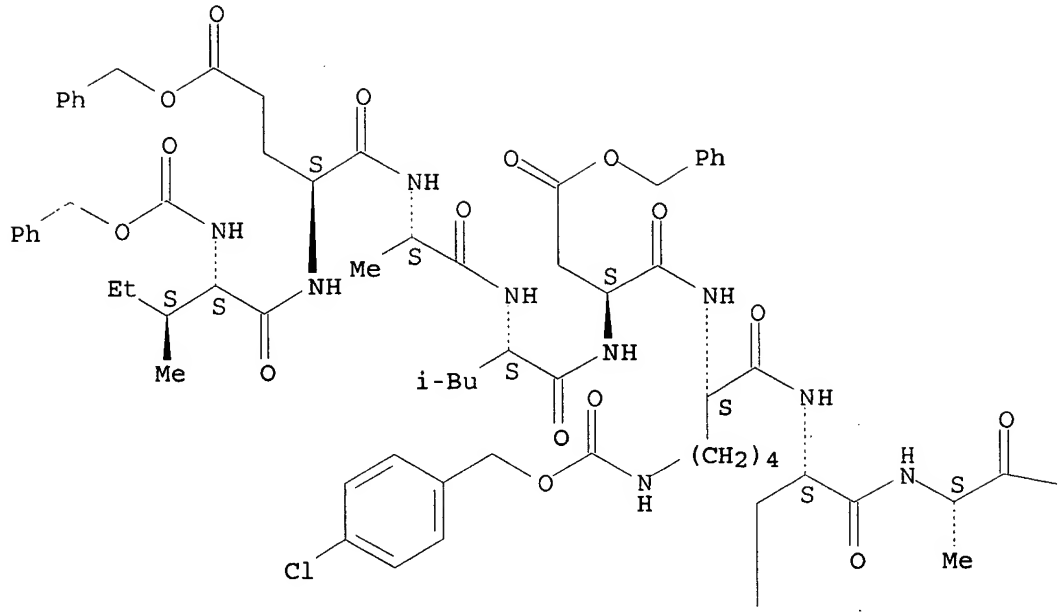
Absolute stereochemistry.



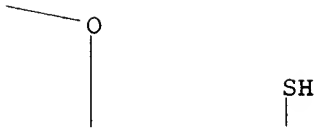
IT 101697-62-5P
RL: SPN (Synthetic preparation); PREP (Preparation)
(prepn. of, by solid-phase method)
RN 101697-62-5 CAPLUS
CN L-Alanine, N-[N-[N6-[[(4-chlorophenyl)methoxy]carbonyl]-N2-[N-[N-[N-[N-[(phenylmethoxy)carbonyl]-L-isoleucyl]-L-.alpha.-glutamyl]-L-alanyl]-L-leucyl]-L-.alpha.-aspartyl]-L-lysyl]-O-[(2,6-dichlorophenyl)methyl]-L-tyrosyl]-, 1-(6-mercapto-4-dibenzofuranyl) 4,5-bis(phenylmethyl) ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.

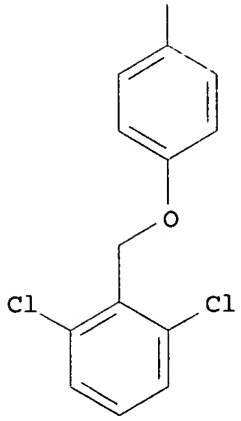
PAGE 1-A



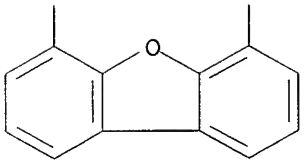
PAGE 1-B



PAGE 2-A



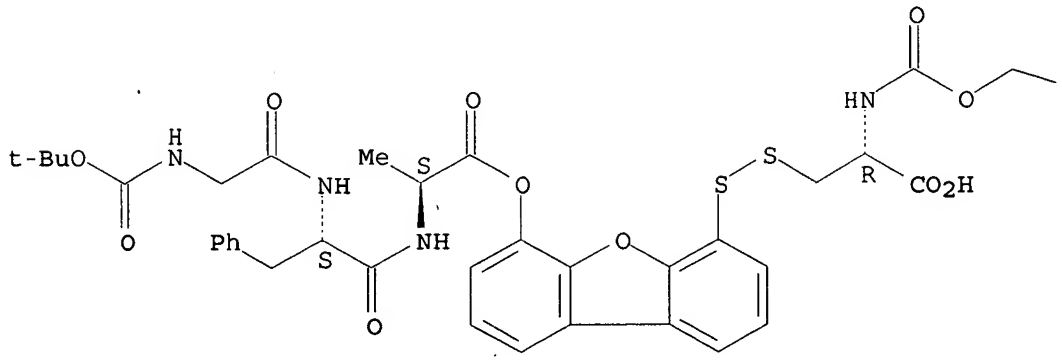
PAGE 2-B



IT 101711-52-8D, resin-bound
RL: RCT (Reactant); RACT (Reactant or reagent)
(solid-phase peptide synthesis with)
RN 101711-52-8 CAPLUS
CN L-Alanine, N-[N-[N-[(1,1-dimethylethoxy)carbonyl]glycyl]-L-phenylalanyl]-, ester with 3-[(6-hydroxy-4-dibenzofuranyl)dithio]-N-[(phenylmethoxy)carbonyl]-L-alanine (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



PAGE 1-B

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